National Institute for Public Health
and the Environment
Ministry of Health, Welfare and Sport

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RIVM Letter report 2018-0018
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Colophon

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Synopsis

Cumulative exposure to residues of plant protection products via food in the Netherlands

People are exposed to residues of different plant protection products via food. This can be due to the consumption of different foods which contain different residues or because more than one residue is present in a food product. RIVM has analysed this so called cumulative exposure to residues from plant protection products via food.

In this study, substances that may affect the thyroid and those that may affect the nervous system were included. The current exposure to these substances is not likely to cause a health effect on the thyroid. With regard to the substances that may affect the nervous system a risk cannot be excluded. This is because the margin between the calculated exposure and the limit that is considered safe is relatively small. The real exposure is most likely lower than the calculated exposure, due to uncertainties in the calculation.

Cumulative exposure assessment is based on the assumption that only substances that affect the same organ should be summed.

To analyse the safety of cumulative exposure to all residues of plant protection products via food, it is necessary to determine which substances should be summed for other organs than the thyroid and nervous system. The European Food Safety Authority (EFSA) is currently working on further grouping of substances. This requires analysis of all the available data on adverse effects of residues in plant protection products.

Keywords: cumulative exposure, young children, children, adults, older adults, plant protection products, probabilistic

Publiekssamenvatting

Gelijktijdige blootstelling aan residuen van gewasbeschermingsmiddelen via voedsel in Nederland

Mensen worden via voedsel blootgesteld aan stoffen uit gewasbeschermingsmiddelen. Dit kan door verschillende soorten voedsel te eten waar verschillende stoffen op zitten, en doordat meerdere stoffen op één soort voedsel kunnen zitten. Het RIVM heeft een inschatting gemaakt van deze gelijktijdige blootstelling aan stoffen uit gewasbeschermingsmiddelen, zogenoemde cumulatieve blootstelling, via voedsel.

In deze studie gaat het om stoffen die effecten op de schildklier en het zenuwstelsel kunnen hebben. De huidige gelijktijdige blootstelling aan deze stoffen heeft geen schadelijke effecten op de schildklier. Voor de stoffen die effect kunnen hebben op het zenuwstelsel kan het RIVM een risico niet uitsluiten. Dat is omdat de marge tussen de hoeveelheid die we binnenkrijgen en de hoeveelheid die als veilig wordt gezien dicht bij elkaar liggen. De werkelijke blootstelling is zeer waarschijnlijk lager dan de berekende blootstelling. Dat komt door onzekerheden in de berekeningen.

Het uitgangspunt van het onderzoek is dat de hoeveelheden van stoffen die op eenzelfde orgaan hun uitwerking hebben, bij elkaar worden opgeteld.

Het is nog niet mogelijk om een uitspraak te doen over de veiligheid van de gelijktijdige blootstelling aan alle stoffen uit gewasbeschermingsmiddelen via voedsel. Hiervoor moet eerst worden bepaald welke stoffen effecten op andere organen dan de schildklier en het zenuwstelsel kunnen hebben. De Europese voedselveiligheidsautoriteit EFSA werkt momenteel aan deze indeling. Hiervoor is een analyse nodig van de beschikbare gegevens over de schadelijke effecten van alle stoffen in gewasbeschermingsmiddelen.

Kernwoorden: gelijktijdige blootstelling, jonge kinderen, kinderen, volwassenen, ouderen, bestrijdingsmiddelen, probabilistisch

Contents

1 Introduction

People are exposed to different residues of plant protection products (PPPs) (or pesticides) via food, either via the consumption of different foods which contain one or more residues of PPPs and/or because more than one residue is present in single food product. This has raised the question whether simultaneous exposure to multiple residues of PPPs via food, so-called cumulative exposure, is safe for consumers.

Over the past years, the European Commission (EC) and its Member States, the European Food Safety Authority (EFSA) and independent scientists have worked on a methodology to estimate cumulative exposure via food (EFSA, 2008; 2009; 2012; van Klaveren et al., 2010). In 2010-2013, the RIVM coordinated the EU project ACROPOLIS; Aggregate and Cumulative Risk Of Pesticides: an On-Line Integrated Strategy[1]. A web-based model was developed to assess cumulative exposure via food (van der Voet et al., 2015) and cumulative exposure assessments were performed for eight European countries (Boon et al., 2015). In addition, EFSA's Panel on Plant Protection Product and their Residues (PPR Panel) has put effort into defining groups of active substances in PPPs that may cause the same toxic effects in tissues, organs and physiological systems – even if they do not share the same mode of action (EFSA, 2013). These groups of substances are called cumulative assessment groups (CAGs). To assess potential risks related to the exposure to such groups of substances via food, a cumulative dietary exposure assessment should be performed. In such an assessment, the exposure to all substances within a CAG via food is estimated. In 2013, the PPR Panel established several CAGs regarding acute and chronic effects on the nervous system and regarding chronic effects on the thyroid (EFSA, 2013).

In 2015, EFSA and RIVM established a Framework Partnership Agreement (FPA). As part of this agreement, RIVM estimated the cumulative dietary exposure to two of the CAGs for acute effects on the nervous system (a CAG for neurochemical effects, i.e. inhibition of acetylcholinesterase activity, and a CAG for effects on the motor division) and two CAGs for chronic effects on the thyroid (one CAG for effects on the parafollicular (C-) cells or the calcitonin system and one CAG for effects on follicular cells and/or thyroid hormone (triiodothyronine-T3 and thyroxine-T4 system). In 2016, EFSA provided an update on the composition of these four CAGs for use in that study, as well as information on the potency of the substances to produce the common effect. To estimate the cumulative exposure to these CAGs, food consumption data from different dietary surveys conducted in European countries and concentration data from European monitoring programmes were used. Data from the Netherlands were included in this study. As this assessment was commissioned by EFSA within the FPA, the results will be published on the EFSA website. Publication is foreseen

[1] acropolis-eu.com

in the second half of 2018. For the other CAGs defined in 2013, no update was provided by EFSA.

In November 2017, a Dutch newspaper[2] published an item about multiple residues on strawberry, entitled *'Strawberries six times more toxic than other fruit due to cocktail effect'*. Questions were raised in the Dutch House of Representatives regarding the methods available for performing a cumulative risk assessment. In response, the Dutch Ministry of Health, Welfare and Sports (VWS) has commissioned RIVM to calculate the cumulative dietary exposure of the Dutch population to the two CAGs regarding acute effects on the nervous system and the two CAGs regarding chronic effects on the thyroid. To this end, RIVM has used the most recent Dutch food consumption data and residue data of PPPs from Dutch monitoring programmes. In this report, the results of this assessment are described.

[2] Trouw, 4 November 2017

2 Exposure calculations

To calculate the exposure to substances present in food, information about the amount and types of foods consumed within the population of interest is needed, as well as information on the concentrations of these substances in the foods consumed. If substances are measured in unprocessed foods, effects of food handling (e.g. peeling and cooking) on the concentration of the substances in the foods as consumed should preferably also be included, if available. Finally, a computational tool is needed to combine these data in such a way that a meaningful estimation of the exposure is obtained.

In this section, the input data and methodology used for assessing the cumulative exposure are described. The methodology used is consistent with the most refined exposure scenario ('tier 2 scenario b') used in the 2017 cumulative study, referred to as the 'FPA study' in the rest of this report.

2.1 Cumulative assessment groups

Cumulative exposure is only meaningful for substances that may cause the same toxic effects in tissues, organs and physiological systems (EFSA, 2013). In this report, the cumulative exposure via food to four of such cumulative assessment groups (CAGs) was calculated; two were defined as having a potential acute effect on the nervous system and two as having a potential chronic effect on the thyroid:

- The CAG covering acute neurochemical effects, i.e. inhibition of acetylcholinesterase activity (CAG-neurochemical);
- The CAG covering acute functional effects on motor division (CAG-motor division);
- The CAG covering chronic effects on parafollicular (C-)cells or the calcitonin system (CAG-calcitonin)
- The CAG covering chronic effects on follicular cells and/or the thyroid hormone (T3/T4) system (CAG-thyroid hormone).

The substances per CAG were provided by EFSA as part of the FPA study and are listed in Appendices A, B, C and D.

2.2 The relative potency factor (RPF) approach

When estimating the exposure to a group of substances, differences in the potency to produce the same toxic effect between the substances within the same group should be considered. For this, the relative potency factor (RPF) approach can be used. In this approach, the potency of the active substances (hereafter referred to as just 'substances') belonging to a CAG is expressed relative to that of one selected substance within the CAG, a so-called "index compound". The potency of a substance reflects its ability to cause harm and is expressed either as a no-observed adverse effect level (NOAEL) or lower limit of a benchmark dose (BMDL), both in mg/kg body weight (bw). The NOAEL reflects the dose at which no adverse effect is observed in an animal toxicity study. The BMDL reflects the dose at which a predefined change (e.g. 5% increase) in an effect occurs in an animal or

epidemiological study. The relative potency of a substance is expressed as a factor of the potency of the index compound. For example, the RPF of a substance is two, when the NOAEL or BMDL of the index compound is twice the NOAEL or BMDL of the substance. See Box 1 for an example of the calculation of an RPF for a substance.

***Box 1**: Calculation relative potency factor (RPF) for carbofuran*
Carbofuran, belonging to the CAG-neurochemical, has a NOAEL of 0.015 mg/kg bw and the index compound oxamyl has a NOAEL of 0.1 mg/kg bw. This results in a RPF of 6.67 for carbofuran. In the calculations, carbofuran is thus considered to be 6.67 times more potent than the index compound oxamyl.

The RPFs per substance are subsequently used to convert single substance concentrations to one cumulative concentration per analysed sample. This adjusted concentration is then used as input for the cumulative exposure assessment. See Box 2 for an example of such a calculation.

***Box 2**: Calculation cumulative concentration of an analysed sample*
A CAG consists of three substances (A, B and C). One food sample has been analysed for all three substances at following concentrations:
A: 0.05 mg/kg; B: 0.10 mg/kg; C: 0.07 mg/kg

The relative potency factors of these compounds are
A: 1; B: 2; C: 0.25.
Substance A is the "index compound".

The cumulative concentration expressed in equivalents of the index compound of this food sample can then be calculated as

$(0.05 \times 1) + (0.10 \times 2) + (0.07 \times 0.25) = 0.27$ mg/kg A equivalents.

In the present study, the RPF approach was used to calculate the cumulative exposure to the four CAGs. The RPFs were provided by EFSA within the FPA study. These RPFs were based on NOAELs, using oxamyl as index compound for the CAGs regarding acute effects on the nervous system. For the CAGs regarding chronic effects on the thyroid, fenbuconazole was used as the index compound for the CAG-calcitonin and ioxynil for the CAG-thyroid hormone. The NOAELs and RPFs per substance and per CAG are listed in Appendices A, B, C and D.

2.3 Food consumption data

To assess the exposure to substances belonging to the four CAGs, food consumption data from the Dutch National Food Consumption Survey (DNFCS) were used. Data were available for three age groups: 2 to 6 years, 7 to 69 years and 70+ years. In the FPA study, only the consumption data of the youngest children (2 to 6 years) were included.

The food consumption data for children aged 2 to 6 were obtained from the DNFCS-Young children conducted in 2005 and 2006 (Ocké et al., 2008). The data for the population aged 7 to 69 were obtained from the DNFCS 2007-2010 (van Rossum et al., 2011), and those for the

population aged 70 + from DNFCS 2010-2012 (Ocké et al., 2013). For a detailed description of the three surveys, see Appendix E.

The food consumption were coded according to the FoodEx1 classification system (EFSA, 2011). FoodEx1 is a hierarchical system based on 20 main food categories that are further divided into subgroups up to a maximum of four levels. Level 4 is the most refined (e.g. bread) and level 1 is the least refined (e.g. grains and grain-based products). The food consumption data were coded at the most refined level as possible, most at level 4. This coding system was used to be in line with the FPA study.

2.4 Residue data

Thirty raw agricultural commodities (RACs), covering widely consumed commodities in the Netherlands were selected for the exposure assessment. These commodities included the 28 commodities to be sampled in 2016, 2017 and 2018 within the EU-coordinated programme (EUCP)[3] (apple, aubergine, banana, beans (with pods), broccoli, carrot, cauliflower, cucumbers, head cabbage, leek, lettuce, mandarin, olives for oil production, orange, peach, pear, peas (without pods), pepper, potato, spinach, strawberry, table grape, tomato, wine grape, oats, rice, rye and wheat) and the two commodities courgette and melon. The commodities included in the assessment were identical to those included in the FPA study.

Only samples analysed as part of EUCP were included, as well as those analysed as part of the Dutch monitoring programme that were randomly, without prior knowledge of high residue levels, sampled. Samples that were taken as part of Regulation (EC) No 669/2009[4], which sets out increased levels of official import control of certain commodities, were also excluded. These commodities are expected to contain higher levels of residues of PPPs based on prior information, such as notifications received through the Rapid Alert System for Food and Feed (RASFF)[5]. Inclusion of these samples in the exposure assessment could potentially result in unrealistically high exposure estimates. The residue data included in the assessment were those sent to EFSA by the Netherlands for the years 2014-2016 according to Article 31 of Regulation (EC) No 396/2005[6]. In the FPA study, residue data from 27 EU Member States, including the Netherlands, and Norway and Iceland were included covering the years 2011-2013.

Based on additional information about the commodities analysed in the residue database, some results were excluded from the exposure

[3] Commission implementing Regulation (EU) 2015/595 of 15 April 2015 concerning a coordinated multiannual control programme of the Union for 2016, 2017 and 2018 to ensure compliance with maximum residue levels of pesticides and to assess the consumer exposure to pesticide residues in and on food of plant and animal origin; OJ L 99.

[4] Commission Regulation (EC) No 669/2009 of 24 July 2009 implementing Regulation (EC) No 882/2004 of the European Parliament and of the Council as regards the increased level of official controls on imports of certain feed and food of non-animal origin and amending Decision 2006/504/EC; OJ L 194.

[5] ec.europa.eu/food/safety/rasff_en

[6] Regulation (EC) NO 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC; OJ L 70.

assessment to avoid erroneous exposure results. These exclusions are described in Appendix F.

When the number of analysed samples for a substance/RAC combination with authorised use was less than 10, these samples were deemed to be too limited to represent the levels of the substance in the RAC as available on the market. These analyses were therefore supplemented by concentration data of the same substance on another comparable RAC. This minimum number of 10 was in accordance with the FPA study. To supplement concentration data, the extrapolation principles for treatments close to harvest were used as described in the EU guidelines on comparability, extrapolation, group tolerance and data requirements for setting maximum residue limits (MRLs) (EC, 2011). For this, it was assumed that the condition of good agricultural practice (GAP) similarity was satisfied when the MRL for the relevant substance/RAC combination was the same for the RAC(s) involved in the extrapolation. For the substance/RAC combinations for which no extrapolation could be performed, the concentration data as such were used in the exposure assessment. The extrapolations applied in this study were mainly related to the limited number of samples analysed for rye and oats. These samples were supplemented by those of wheat. For a limited number of substances, the measurements in wine grape and aubergines were supplemented by those in table grape and tomato, respectively.

The residue data were expressed according to the legal residue definition for enforcement and monitoring, and used as such in the exposure assessment. Additionally, residue data of complex residue definitions covering more than one active substance were assumed to relate to the presence of the least potent of the authorised substances on the respective commodity (which can be a substance not included in the CAG) or to any eventual metabolite produced by these active substances when this metabolite is of lower potency. Footnotes per relevant substance in Appendices A, B, C and D indicate what this meant for this study.

The residue data were coded according to the Standard Sample Description (SSD) format. According to this format, the RACs analysed are coded using the matrix code. This code is based on the coding used in Annex I of Regulation (EC) 396/2005, last amended by Regulation (EU) No 62/2018[7].

Appendices G, H, I and J provide an overview of the residue data of the substances belonging to the four CAGs.

2.5 Drinking water

A potential source of dietary exposure to residues of PPPs is drinking water (EFSA, 2012; Swartjes et al., 2016). This source of exposure should therefore also be considered in a cumulative exposure assessment. As no residue data were available for drinking water, this source was considered by assuming that the five most potent

[7] Commission regulation (EC) No 2018/62 of 17 January 2018 replacing Annex I to Regulation (EC) No 396/2005 of the European Parliament and of the Council; OJ L 18.

substances per CAG were present at a level of 0.05 µg/L. This level is equal to half the drinking water standard for individual residues of PPPs according to the Dutch Drinking Water Law[8].

One single water sample for each of the five substances per CAG was therefore added manually to the residue dataset. The substances for which this was done were

- carbofuran, methiocarb, formetanate, oxamyl and pirimicarb for the CAG-neurochemical;
- oxamyl, methiocarb, omethoate, fluquinconazole and cyfluthrin for the CAG-motor division;
- carbofuran , profenofos, ioxynil, ipconazole and fenamidone for the CAG-calcitonin;
- ioxynil, fipronil, propineb, amitrole and mepanipyrim for the CAG-thyroid hormone.

2.6 Linking foods analysed to those consumed

Residue data of PPP substances are predominantly analysed in raw agricultural commodities (RACs), whereas food consumption data are collected on foods as consumed. To link these two entities, the food conversion model delivered to EFSA in 2011 (Boon et al., Unpublished) was used. The basis for this food conversion model is the Dutch food conversion model (Boon et al., 2009; Geraets et al., 2011; van Dooren et al., 1995). This model was used because it converts foods coded at FoodEx1 (section 2.3) to RACs coded using the matrix code (section 2.4). The food conversion model was extended to include consumed foods containing water as an ingredient (Appendix K). This was only done for consumed foods to which water was added 'at home', namely tea, coffee, lemonade and soup.

Some RACs (and drinking water) are consumed as such. This is, for example, the case for apples, pears and cucumbers. These RACs could therefore be linked directly to their consumed amounts as recorded in the food consumption databases. To also include the exposure via the consumption of processed and composite foods, such as apple juice, pizza and apple pie, the consumption of these foods was converted to equivalent consumptions of individual RACs. This was done based on recipe data and/or food conversion factors of processed ingredients to their raw counterparts. For example, pizza was first divided into equivalent amounts of its ingredients, such as flour, onion and tomato, based on recipe data. These ingredients were subsequently converted to their raw counterparts (wheat, onion and tomato, respectively) using food conversion factors. Apple juice, which consists for 100% of apple, only the food conversion step was used to convert its consumption to its equivalent amount of raw apple. As part of the conversion also the processing type per RAC was identified to include possible effects of food handling on residues of PPPs in the exposure assessment (section 2.7).

Apart from residue data in RACs, the residue database also contained some residue levels analysed in foods as consumed. These samples

[8] Richtlijn 98/83/EG van de Raad van 3 november 1998 betreffende de kwaliteit van voor menselijke consumptie bestemd water.

could be linked directly to their consumed amounts as recorded in the food consumption survey. This was true for olive oil and wine. The consumption of foods for infants and young children (belonging to FoodEx 1 group A.17) could also be linked directly to analysed infant foods (Appendix L).

The residue database also contained concentrations of substances in fruit juices. These results were however not included in the exposure assessment, because the number of analysed samples was too limited. The exposure through the consumption of fruit juices was therefore included via the residue levels analysed in the raw fruits using the food conversion model. The same approach was followed for residues in some processed cereals which were also too limited for use in the assessment.

2.7 Effect of food handling on residue levels

RACs are typically consumed after some form of food handling, such as peeling or cooking. Concentrations of substances may be affected by this and therefore processing factors should be included in an exposure assessment when dealing with substances that are (predominantly) analysed in RACs and when the aim is to provide the most realistic exposure estimate possible. A processing factor is the ratio of the residue level in the processed commodity divided by the residue level in the raw commodity. Processing factors depend on food, processing type and substance.

In the present study, the same processing factors were used as those in the FPA study. These processing factors were exclusively collected from EFSA's Reasoned Opinions[9] covering the period until the end of July 2015. Additional processing factors were collected in this study for substance/RAC combinations that contributed largely to the cumulative exposure from EFSA conclusions on active substances, reports of the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) published until September 2016 and the processing database of the German Federal Institute for Risk Assessment (BfR)[10].

Processing factors include both the effects from chemical alteration of the substance and from weight changes of the food (e.g. loss of water due to drying). However, the latter alterations relate to changes in the food itself and are already accounted for via the food conversion model (section 2.6). Processing factors were therefore corrected so that they only included the effect of processing on chemical alterations. For an example of such a correction, see Box 3.

[9] Reasoned opinions in application of Article 12 of Regulation (EC) No 396/2005 and subsequently further MRL applications submitted for the respective active substance under Article 10 to the same regulation.
[10] Bundesinstitut für Risikobewertung (BfR) Data Collection on Processing Factors http://www.bfr.bund.de/cm/349/bfr-compilation-of-processing-factors.xlsx

Box 3: *Correction of processing factor for food conversion factor*
The ratio of the presence of substance A in raisins to table grapes is 5 (= processing factor). In the food conversion model, the conversion factor of table grapes to raisins is 3.1. This means that you need 310 grams of table grapes to obtain 100 grams of raisins.

The corrected processing factor used in the exposure assessment will then equal $\frac{5}{3.1}$ = 1.6.

An overview of the processing factors used in the present study is listed in Appendix D of the report of the FPA study.

2.8 Handling of left-censored data

Residue data of PPP substances often contain samples having an analysed level below the limit of quantification (LOQ), the so-called left-censored samples. In these samples, it is not clear if the substance is present but at such a level that it cannot be quantified by the analytical method or that it is not present. To assign a concentration to these samples, preferably use frequency data are used. Use frequency data provide information about the expected presence of a substance on a RAC in a particular year and region, based on information about the use of PPPs by, for example, growers. Use frequency data can be used as follows. When these data suggest that a PPP containing the relevant substance may be used on 10% of the apples available on the market, 10% of the residue levels below LOQ in apple of this substance can be replaced with a specified level below the LOQ (e.g. ½LOQ), assuming that the substance is present. The remaining 90% of the residue levels below LOQ in apple can then equally be considered to not contain the substance based on these use data.

Unfortunately, use frequency data are not (readily) available. Therefore, the information available in the residue database was used to derive a 'substitute' use frequency per substance/RAC combination. Use frequency was defined as the ratio of the samples having a quantifiable concentration of the substance and the total number of samples analysed for this substance over the period of interest. Appendices M, N, O and P present an overview of the input parameters for the calculation of the use frequency per substance/RAC combination for the substances belonging to the four CAGs. Based on these use frequencies, either zero or a level equal to ½LOQ was assigned to the left-censored samples. Box 4 provides an example how this was done.

Box 4: *Example of how residue levels were assigned to left-censored samples.*
Two out of the 249 analysed orange samples had a positive residue level for phosmet (Appendix E). The corresponding use frequency for this substance/RAC combination equalled therefore 0.008 (=2/249). Thus, the 247 remaining left-censored samples were assigned a zero concentration with a probability of 99% and ½LOQ with a probability of 1%.

2.9 Missing values

Ideally, all samples analysed within a monitoring programme are measured for all substances belonging to a CAG. In reality however, this is not true, and samples may have 'missing values'. For example, 249 out of the 315 orange samples analysed in the period 2014-2016 were analysed for phosmet (Appendix G). To avoid underestimation of the exposure by assuming that these samples do not contain the substance, these missing values were also imputed based on the information on use frequencies (section 2.8). Imputation of the missing values was only performed for the acute CAGs: in a chronic assessment only a mean concentration per RAC/substance combination is needed (section 2.11).

2.10 Unit variability

Substances of PPPs are typically analysed in samples consisting of more than one unit of a RAC (e.g. apples are analysed in samples consisting of 12 units each). Because residue levels may vary between individual RAC units, consumers may be confronted with higher levels when consuming single units (e.g. one apple) than the average residue level analysed in a sample. To account for this possibility, unit variability factors are used in acute dietary exposure assessment. Unit variability is relevant for RACs having a unit weight larger than 25 grams (medium and large unit size). Examples of such RACs are apples, oranges, cauliflower and carrot.

To model the residue levels in individual units, information on the variability factor, unit weights of RACs and the number of units in a composite sample is needed.

Variability factors
A variability factor of 3.6 was used for all RACs having a unit weight larger than 25 grams. This variability factor is the average factor observed in market samples as reported in an opinion of EFSA's PPR Panel on the use of the appropriate variability factor(s) for acute dietary intake assessment of pesticide residues (EFSA, 2005b).

Unit weights
The unit weights of the EFSA PRIMo – Pesticide Residue Intake Model database (EFSA, 2018b), available at the EFSA website were used.

Number of units in a sample
The number of units in an analysed sample was assumed to equal twice the minimum number as specified in the EU sampling Directive EC 2002/23[11]. This meant that the number of units equalled 20 for RACs having a unit weight between 25 and 250 grams, and 10 for RACs having a unit weight above 250 grams.

For an overview of the unit weights and number of units in a sample used per RAC, see Appendix Q. Unit variability is only relevant for

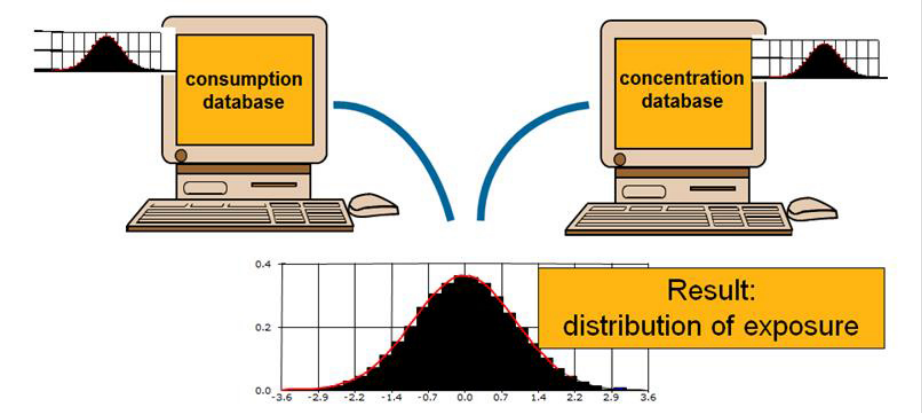
[11] Commission Directive 2002/63/EC of 11 July 2002 establishingCommunity methods of sampling for the official control of pesticide residues in and on products of plant and animal origin and repealing Directive 79/700/EEC; OJ L 187.

calculating the exposure to the two CAGs covering acute effects on the nervous system.

2.11 Cumulative exposure assessment

Different methodologies are available to calculate the exposure to substances present in food, ranging from simple deterministic models (e.g. the EFSA Pesticide Residue Intake Model (PRIMo) used to assess the acute and chronic exposure to single residues of PPPs (EFSA, 2018b)) to probabilistic models. In deterministic models, summary statistics, such as a mean, median and/or high(est) level, of food consumption and concentration data are combined, resulting in a single estimate (typically, a mean or high level) of exposure. In probabilistic models, the whole food consumption and concentration database are used as input resulting in a distribution of exposure (Box 5). This distribution reflects the differences in exposure between individuals within a population due to differences in food consumption patterns and in residue levels within (acute) and between (acute and chronic) foods.

Box 5: *Probabilistic modelling of dietary exposure*



A probabilistic approach is needed to estimate the exposure to many substances via the consumption of many foods (EFSA, 2012). With this methodology, concentrations of different substances in many foods as well as correlations between concentrations of different substances in the same food sample are taken into account simultaneously. Also the consumption of many foods and correlations between foods consumed on a certain day (e.g., it is not likely that a person consumes endive and spinach on the same day, but may consume head cabbage in combination with cucumber and tomato) are included. Deterministic models cannot consider all these input data at the same time in a meaningful way. In the EU 7th Framework project ACROPOLIS, a tool was developed to estimate cumulative exposure using a probabilistic approach (van der Voet et al, 2015), which has since been optimised further to make it suitable for assessing the cumulative exposure to large CAGs, consisting of up to a 100 substances (van der Voet et al., 2016). This tool is the Monte Carlo Risk Assessment (MCRA) software (release 8.2), which was used in this report for assessing the cumulative exposure to the four CAGs (de Boer et al., 2016; van der Voet et al., 2015; 2016).

The common toxic effects of the four CAGs included two acute effects on the nervous system and two chronic effects on the thyroid (section 2.1). Acute and chronic effects require the calculation of the acute and chronic exposure, respectively. Acute exposure relates to the exposure on an arbitrary day and, depending on the amounts of the relevant foods consumed and residue levels present in foods, can vary significantly from day to day within a person. Chronic exposure, on the other hand, relates to the average exposure over a longer period of time. In this type of assessment, variations in exposure between days within an individual are not relevant, as variations are expected to level out on the long-run.

The acute cumulative exposure was calculated by multiplying randomly drawn daily consumption patterns of foods from the food consumption database by randomly drawn sample based cumulative concentrations expressed in equivalents of the index compound (Box 2; section 2.2). This was done a 100.000 times. The resulting cumulative exposures per food per person-day were summed across foods resulting in a distribution of 100.000 cumulative daily acute exposure estimates (Box 5).

The chronic cumulative exposure was calculated using the observed individual means (OIM) approach within MCRA. In this model, daily food consumption patterns of individuals obtained from the food consumption database were multiplied by the sample based mean cumulative residue level per food and summed over foods per day per individual. Subsequently, the daily individual exposures were averaged over the two consumption days per individual, resulting in a distribution of two-day-average exposure levels per individual.

The exposure estimates were divided by the individual body weights. The exposure distributions of young children and persons aged 7 to 69 were furthermore weighted for small deviances in socio-demographic factors and season. The exposure distribution of this last age group was also corrected for day of the week[12]. The exposure distribution of the persons aged 70+ were corrected for small differences in sex, age, region, level of urbanisation, day of the week and season as compared to the community-dwelling older Dutch adults. Weights were those used by Ocké et al. (2008; 2013) and van Rossum et al. (2011). For more detailed information about the cumulative exposure assessment within MCRA, see de Boer et al. (2016).

Information on use frequencies was used to assign zero or ½LOQ to left-censored samples (section 2.8), as well as to impute missing values (sections 2.9; Appendices M, N, O and P). Processing factors were included as a fixed factor by multiplying the factor by the relevant residue level per substance/RAC/processing combination (section 2.7). The effect of processing was included before calculating the cumulative concentration per analysed sample using RPFs (Box 2; section 2.2).

[12] So that the data equally represented all days of the week

In the acute assessment, residue levels in single units were calculated based on the mean residue levels in analysed samples. This was done using the input data described in section 2.10, and assuming that the unit residue levels within an analysed sample follow a beta distribution. Using this distribution, it is assumed that the simulated unit residue levels are never higher than the residue level of the analysed sample times the number of units in the sample (i.e. the worst case is that one single unit contains all the substance within the sample). Unit variability was modelled for residue levels analysed in all RACs, except for those analysed in cereals, beans (with pods), olives (for oil production), peas (without pods), spinach, strawberry and wine grape. These RACs have a unit weight equal to or less than 25 grams.

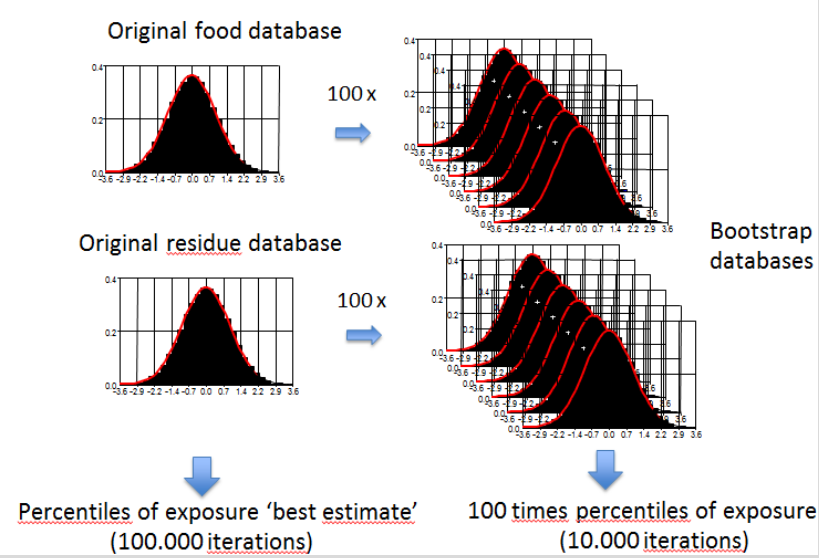
The exposure was expressed in different percentiles of the cumulative exposure distribution, namely P50 (median), P90, P95, P99, P99.9 and P99.99 for four age groups: 2 to 6, 7 to 17, 18 to 69 and 70+ years. These age groups were selected to address possible differences in exposure, due to differences in food consumption patterns between age groups, and in consumption amounts per kg body weight. Young children are, for example, known to have higher exposure levels than adults because of higher consumption levels per kg body weight. Also the contribution of the RACs, the substances and substance/RAC combinations to the cumulative exposure were calculated per age group and CAG. In the FPA study, the exposure for the Netherlands was estimated for children aged 2 and children aged 3 to 6.

The uncertainty in the exposure due to the limited size of the food consumption and residue databases was calculated using the bootstrap approach. For more information about the bootstrap approach, see Box 6. The uncertainty was reported as the 95% confidence interval around the best estimates of the exposure percentiles. Such a confidence interval means, considering the uncertainty addressed, that there is a 95% probability that the real exposure percentile falls within this interval, and thus that there is a 5% probability that the calculated percentiles may be outside the interval: 2.5% probability each that the real exposure percentile is lower or higher than the lower or upper limit of the confidence interval, respectively. The exposure was also influenced by other sources of uncertainty. These are described and evaluated qualitatively according to the format proposed by EFSA (2006; 2012) in section 5.

Box 6: *Bootstrap approach*

To quantify the uncertainty in the exposure estimates due to the limited size of the food consumption and residue databases, the bootstrap approach can be used (Efron, 1979; Efron & Tibshirani, 1993). With this method, a bootstrap database is generated of the same size as the original database for both the food consumption and concentration database by sampling with replacement from the original datasets. These bootstrap databases are considered as databases that could have been obtained from the original population if another sample was randomly drawn. These two bootstrap databases are then used for the exposure calculations and derivation of the relevant percentiles. Repeating this process many times results in a bootstrap distribution for each percentile that allows for the derivation of confidence intervals around it. The bootstrap approach was used in this report by generating 100 food consumption and 100 concentration bootstrap databases and calculating the cumulative acute (with 10,000 iterations each) exposure. Of the resulting bootstrap distributions per percentile a 95% uncertainty interval was calculated by computing the 2.5% and 97.5% points of the empirical distribution.

Note that by bootstrapping both the consumption and concentration database in one analysis it is not possible to quantify which part of the uncertainty was due to a limited number of consumption or concentration data.



3 Risk characterisation

To determine whether the calculated exposures could result in a potential health risk, a risk characterisation should be performed. For this, the calculated exposures are typically compared with a health-based guidance value (HBGV), such as the acceptable daily intake (ADI) for chronic exposure or acute reference dose (ARfD) for acute exposure, or a margin of exposure (MOE) is calculated. As guidance on how to perform a risk characterisation of cumulative exposure is not yet available, the MOE approach was used in this report. This approach provides a quantitative measure of the margin between a 'safe intake level' and the calculated exposure.

MOEs were calculated per CAG by dividing the NOAEL ('safe intake level') of the relevant index compound by the different percentiles of exposure (section 2.11). The NOAEL of oxamyl equalled 0.1 mg/kg bw for the CAGs covering effects on the nervous system (Appendices A and B). For the CAGs covering effects on the thyroid, the NOAELs for fenbuconazole (CAG-calcitonin) and ioxynil (CAG-thyroid hormone) were 3 and 0.02 mg/kg bw, respectively (Appendices C and D). See Box 7 for an example how the MOE is calculated.

Box 7: *Example of the calculation of a margin of exposure*
The index compound of the CAG-neurchemical is oxamyl with a NOAEL of 0.1 mg/kg bw. Assuming that the P95 of exposure to this CAG equals 0.02 mg/kg bw per day, the margin of exposure (MOE) would equal $\frac{0.1}{0.002} = 50$.

This means that the exposure to this CAG at the P95 level of the exposure distribution is 50 times lower than the NOAEL of the index compound.

The MOE can have the following outcomes:
MOE = 1: the exposure equals the NOAEL
MOE < 1: the exposure is higher than the NOAEL
MOE > 1: the exposure is lower than the NOAEL

The results of the exposure calculations, including the lower and upper limit of the 95% confidence interval, are expressed in MOEs.

4 Results

4.1 Two CAGs covering acute effects on the nervous system

4.1.1 CAG covering neurochemical effects

Margins of exposure

Table 1 lists the best estimates of the margins of exposure (MOEs) for the P99, P99.9 and P99.99 of dietary exposure for the CAG covering neurochemical effects, including the lower and upper limits of the 95% confidence interval. The MOEs of the percentiles of exposure up to the P95 were all higher than 500 (including those at the lower limit of the confidence interval). See Appendix R for an overview of the calculated MOEs.

The best estimates of the MOEs ranged from 31 in children aged 2 to 6 at the P99.99 to 1355 in the 70+ age group at the P99 (Table 1). Considering the quantified uncertainty in the estimated MOEs, the MOE could be as low as 280 for the P99, 54 for the P99.9 and 21 for the P99.99, all in the youngest age group (Table 1).

Table 1. Margins of exposure per exposure percentile for the CAG covering neurochemical effects

Age (years)	Margins of exposure per exposure percentile		
	P99	P99.9	P99.99
2-6	396 (280 – 567)	116 (54 – 181)	31 (21 -82)
7-17	881 (707 – 1245)	254 (167 – 379)	109 (52 – 214)
18-69	1192 (998 – 1601)	331 (166 – 571)	114 (74 – 285)
70+	1355 (1058 – 1727)	240 (89 - 536)	62 (39 – 225)

CAG: cumulative assessment group

Contribution RACs, substances and substance/RAC combinations to the upper 0.1% of the cumulative exposure distribution

As health risks related to the exposure to substances of PPPs predominantly occur in the upper part of the exposure distribution, the contribution of the different parameters to the upper 0.1% of the acute cumulative exposure distribution to CAG-neurochemical was calculated.

The cumulative exposure in this part of the exposure distribution was completely dominated by the consumption of spinach. The contribution of this commodity ranged from 30% in 7 to 17-year olds to up to 67% in young children and persons aged 70+. The substance contributing most to this upper part was pirimicarb in all age groups: 50 – 82%. The substance/RAC combination contributing was thus pirimicarb in spinach with contributions ranging from 30% to 67%. An important second contributor was the presence of methiocarb on beans (with pods) in the three older age groups: 24-25%. Other contributions of at least 10% were methiocarb in table grape (12%) and pirimicarb in strawberry

(11%) in children aged 7 to 17, and pirimicarb in apple (10%) in the youngest age group.

See Appendix S for an overview of the contribution of RACs, substances and substance/RAC combinations to the upper 0.1% of the exposure distribution per age group.

4.1.2 *CAG covering effects on motor division*

Margins of exposure

Table 2 lists the same information as Table 1, but now for the CAG covering effects on motor division. The MOEs of the percentiles of exposure up to the P95 were all higher than 1500 (including those at the lower limit of the confidence interval). See Appendix R for an overview of the calculated MOEs.

The best estimates of the MOEs ranged from 209 in children aged 2 to 6 at the P99.99 to 2903 in the adult age group at the P99 (Table 2). Considering the quantified uncertainty in the estimated MOEs, the MOEs could be as low as 935 at the P99, 327 at the P99.9 and 144 at the P99.99, all in the youngest age group (Table 2).

Table 2. Margins of exposure per exposure percentiles for the CAG covering effects on motor division

Age (years)	Margins of exposure per exposure percentile		
	P99	P99.9	P99.99
2-6	1192 (935 – 1431)	415 (327 – 567)	209 (144 – 343)
7-17	1932 (1374 – 2464)	716 (546 – 932)	326 213 – 577)
18-69	2903 (2196 – 3550)	1065 (813 – 1486)	512 (352 – 962)
70+	2706 (2006 – 3317)	868 (610 – 1255)	443 (353 – 895)

CAG: cumulative assessment group

Contribution RACs, substances and substance/RAC combinations to the upper 0.1% of the cumulative exposure distribution

The consumption of table grape, spinach, potato and beans (with pods) contributed more than 10% to the upper 0.1% of the acute cumulative exposure distribution in at least one of the age groups.

The dominant substance contributing to the upper 0.1% of the exposure distribution was lambda-cyhalothrin in all age groups with contributions ranging from 43% in the 7 to 17-year olds up to 66% in the oldest age group. Other substances that contributed for at least 10% were deltamethrin (17%) and methiocarb (12%) in young children, chlorpropham (11-25%) and methiocarb (11-13%) in children aged 7 to 17 and the adult age group, and deltamethrin (18%) in persons aged 70+.

Lambda-cyhalothrin in table grape, beans (with pods) and spinach, deltamethrin in spinach and chlorpropham in potato contributed at least 10% to the upper 0.1% of the cumulative exposure distribution in at least one of the age groups.

Appendix T provides an overview of the contribution of RACs, substances and substance/RAC combinations to the upper 0.1% of the exposure distribution per age group.

4.2 Two CAGs covering chronic effects on the thyroid

Below we report on the MOEs of exposure for the CAGs covering chronic effects on the thyroid (Table 3). Since these MOEs were larger than 500, even at the highest calculated percentile (P99.99), contributions of the RACs to the upper part of the exposure distribution are not reported below. Also for these CAGs, the MOEs for the three highest percentiles of exposure were reported. See Appendix R for an overview of the calculated MOEs.

Table 3. Margins of exposure per exposure percentile for the CAGs covering effects on parafollicular (C-)cells or the calcitonin system on follicular cells and/or the thyroid hormone (T3/T4) system

Age (years)	Margins of exposure per exposure percentile		
	P99	P99.9	P99.99
CAG-calcitonin			
2-6	1729 (1445 – 1981)	1049 (922 – 1358)	903 (726 – 1143)
7-17	3156 (2778 - 3484)	2286 (2139 – 2720)	2092 (1989 – 2597)
18-69	2716 (2404 – 3045)	2112 (2004 – 2226)	1929 (1821 – 2196)
70+	3625 (3421 – 3916)	2949 (2806 – 3411)	2791 (2743 – 3264)
CAG-thyroid hormone			
2-6	6824 (4475 – 10270)	3126 (2151 – 5849)	3054 (2047 – 4625)
7-17	12820 (9208 – 16840)	7202 (4695 – 11470)	6043 (4343 – 9369)
18-69	17620 (11960 – 21590)	10710 (5410 – 15640)	6118 (3939 – 13240)
70+	17330 (11700 – 24090)	13110 (8047 – 18170)	10580 (7278 – 17180)

CAG: cumulative assessment group

The best estimates of the MOEs ranged from 903 at the P99.99 in the youngest age group to 3625 at the P99 in the 70+ age group for the CAG-calcitonin (Table 3). Corresponding numbers for CAG-thyroid hormone were 3054 at the P99.99 in the youngest age group and 17620 at the P99 in the adult age group. Considering the quantified uncertainty in the estimated MOEs, the lowest MOEs for the CAG-calcitonin and CAG-thyroid hormone were 726 and 2047, respectively, for the P99.99 of exposure in the youngest age group.

5 Uncertainties in the cumulative exposure assessment

The cumulative exposure assessment of all four CAGs was influenced by different sources of uncertainty. The most important sources are discussed in detail below.

5.1 Food consumption data

The food consumption data used in the cumulative exposure assessment were the most recent data available for the Netherlands (Appendix E). However, especially the food consumption data of children aged 2 to 6 were collected more than 10 years ago. Presently, a new food consumption survey is being conducted among persons aged 1 to 79. Preliminary results of this survey collected in the period of 2012-2014 show that consumption patterns are changing[13]. A relevant change regarding this report is that the fruit consumption in children aged 7 to 18 has increased. However, the consumption of vegetables and cereals seems not to have changed since the previous food consumption survey.

If the fruit consumption is indeed increased, in part or the total population, the present estimates of exposure may underestimate the exposure to a certain extent. When the new data come available and confirm these changes in food consumption patterns, or show that also the consumption of vegetables and cereals has increased, it may be advisable to repeat the calculation. This would be most relevant for the CAG covering neurochemical effects, because the exposure to this CAG resulted in the lowest margins of exposure (Table 1).

Another important factor to take into account when estimating the exposure to substances present in food is that habitual eating patterns may be influenced or changed due to the recording process. Foods that are known to be healthy like fruits and vegetables may be eaten more on recording days than usually. If true, this may have resulted in an overestimation of the calculated exposure to residues of PPPs, which are mainly present in these healthy foods. The extent in which eating habits are changed due to the recording process and consequently the effect on calculated exposure levels is unknown. Another potential source of overestimation could have been the underreporting of body weight in the food consumption surveys. This source of overestimation is only relevant for the age group of 7 to 69: in the young children and 70+ surveys body weight was measured (Ocké et al., 2008; 2013; van Rossum et al., 2011). The extent in which body weights were underreported was not investigated (van Rossum et al., 2011).

To be in line with the FPA study, the FoodEx1 coding system was used to match foods consumed to those analysed. The FoodEx1 system is a less detailed coding system than the one of the Dutch Food Composition

13 www.rivm.nl/Onderwerpen/V/Voedselconsumptiepeiling/Overzicht_voedselconsumptiepeilingen/VCP_Basis_1_79_jaar_2012_2016

Database NEVO[14], the food coding system that could also have been used in this study[15]. For vegetable products consumed as such, it is estimated that the error will be negligible as these foods are predominantly coded at the highest (detailed) level of FoodEx1. For composite foods, this is less certain. FoodEx1 has only broad codes for composite foods and it can therefore not be ruled out that the use of the more detailed NEVO food codes would have resulted in a better match between the foods consumed and analysed. As less precise matching will typically result in more conservative estimates of exposure, because of conservative choices during linkage, the use of FoodEx1 may have resulted in an overestimation of the exposure.

5.2 Residue data

Monitoring data were used to calculate the cumulative exposure (section 2.4). By selecting only the samples that were randomly sampled for inclusion in the exposure assessment, bias of the exposure to higher exposure levels was minimised as much as possible. However, despite this, it is generally known that monitoring data may not be representative of the foods available on the market and are likely to be biased to those commodities that are expected to contain PPP residues. Therefore, even though samples were not taken with any prior knowledge of the presence of residues, overestimation of the exposure by using monitoring data cannot be ruled out completely. However, monitoring data are the best, and often the only data available for assessing the acute exposure, both to single and multiple substances. For acute exposure, residue levels per product are needed, making for example data of Total Diet Studies (TDS) not suitable for acute exposure assessment purposes (EFSA et al., 2011). TDS concentration data relate to foods as consumed and represent therefore potentially better the levels to which people are exposed than monitoring data. However, TDS data are average concentrations of substances in food, and therefore not suitable for use in an acute exposure assessment. For this type of assessment, concentrations in individual foods are needed to reflect the daily variation in residue levels in foods (section 2.11). TDS data are however suitable to calculate chronic exposure, because for this type of exposure average residue levels per food are used (section 2.11). However, no TDS data on residues of PPPs were available for products available on the Dutch market.

In monitoring programmes, not all samples are analysed for all substances belonging to a CAG (section 2.9). Because this does not mean that the substance is not present, residue levels were assigned for the calculation of the cumulative sample concentration to minimise the possible underestimation of the exposure. Preferably, this should be based on knowledge about the actual use of PPPs, for example obtained from growers. As this information is not (readily) available, residue levels were assigned based on use frequency data per substance/RAC combination obtained from the residue database (section 2.8). Use frequency was defined as the number of samples with a positive residue

[14] nevo-online.rivm.nl/

[15] The Dutch food consumption data are also coded at an ever more refined level than NEVO, namely by EPIC-Soft. However, these codes are not part of the Dutch food conversion model for mapping foods consumed to RACs.

level divided by the total number of samples analysed per substance/RAC combination. As an alternative approach, it could have been assumed that residues were either not present or that they were always present at a certain positive level. This would very likely have resulted in either a very optimistic or conservative estimate of exposure, respectively. Using use frequency data, a more informed choice of presence or non-presence was possible, resulting in a better estimate of the exposure. The same was true for assigning a residue level to the samples with an analysed residue level below the limit of quantification (LOQ), the left-censored samples (section 2.8). Also here, the assumption could have been that these samples do either not contain the residue or the residue is present at (a fraction of the) LOQ, instead of using use frequency data to assign a residue level. As PPPs are not used on all commodities available on the market, the latter option would again have resulted in a conservative exposure estimate, whereas assuming that all left-censored samples do not contain the residue would have been too optimistic. How well the use frequency data used in this study reflect the real use frequency data of PPPs in the field is very uncertain, as no information is available. This approach could have resulted in a under- or overestimation of the exposure. Availability of information about the use of PPPs by for example growers will reduce this uncertainty.

In this assessment, 30 RACs were included. These 30 RACs formed the majority of the vegetable products consumed in the Netherlands, including for example apple, potato, wheat, cauliflower, carrot, etc. This selection is therefore judged not to have resulted in an underestimation of the cumulative exposure to all four CAGs.

Another source of uncertainty related to the residue data were the residue levels in drinking water. As no monitoring data were available for this source and exposure via drinking water cannot be excluded (EFSA, 2012; Swartjes et al., 2016), possible exposure via drinking water was considered using an assumed presence of five substances per CAG at 0.05 µg/L (section 2.5). This is equal to half the drinking water standard for single residues of PPPs according to the Dutch Drinking Water Law. The sum of the single residues should not exceed 5 µg/L according to this law. Based on a Dutch study into the presence of residues of PPPs in groundwater resources of drinking water wells (Swartjes et al., 2016), the assumption about the presence of residues in drinking water in this study has very likely resulted in an overestimation of the exposure via drinking water. Use of analytical data will reduce this source of uncertainty.

In a cumulative risk assessment, the potential contribution of metabolites and degradation products to the specific effects should be taken into account (EFSA, 2018a). As information of residue definitions of active substances related to the common effect is lacking, the residue definition of enforcement and monitoring was used, as in the FPA study. To assess whether this has resulted in an over- or underestimation of the cumulative exposure per CAG, the residue definitions per substance should be examined in relation to the same toxic effect in the organ. Additionally, residue data referring to complex residue definitions for enforcement and monitoring were assumed to relate to the presence of

the least potent authorised substance or metabolite produced (section 2.4). This is a potential source of underestimation of the exposure to the four CAGs like in the FPA study. As the number of substances with a complex residue definition was limited for the CAG-neurochemical and CAG-calcitonin (Appendices A and C), the effect on the exposure to these two CAGs is expected to be limited. For the other two CAGs, the number of substances with a complex residue definition was however larger (Appendices B and D). An underestimation of the exposure to these two CAGs is therefore likely.

5.3 Processing and modelling unit variability

In this assessment, the same processing factors were used as in the FPA study. The information on the effect of processing was very limited, because of the large number of possible substance/RAC/processing types combinations included in the exposure assessment of the four CAGs. For example, there was no processing information available for pirimicarb in spinach and methiocarb in beans (with pods), important contributors to the exposure to the CAG-neurochemical; the CAG with the lowest margins of exposure (section 4.1.1). For pirimicarb in apple, an important contributor to the exposure in young children for this CAG, processing factors were present for the processing types 'sauce / puree' (0.5) and 'juicing' (0.745). However, the majority of apple consumed in this age group was raw (with or without peel). As processing mainly results in a decrease of the residue levels in the processed food compared to the raw product, except for processing types in which commodities are concentrated (e.g. drying and oil extraction), including processing only to a limited extent in the assessment will have resulted in an overestimation of the exposure.

In the present assessment, a mean variability factor of 3.6 was used as observed in market samples (section 2.10). The EFSA guidance on probabilistic modelling does not give direction on which variability factor to use in an acute probabilistic exposure assessment using monitoring data (EFSA, 2012). In deterministic approaches to estimate acute exposure to single compounds, EFSA uses five and seven (EFSA, 2018b), whereas JMRR uses three (FAO/WHO, 2017). Based on the information available, a variability factor of 3.6 was estimated to reflect best the true variability within samples obtained in monitoring programmes. Boon et al. (2015) estimated the cumulative exposure to a selected group of residues of PPPs of the triazole group for a number of European countries according to EFSA guidance on probabilistic modelling. In that study, a variability factor of five was used, and the authors argue that because this factor is higher than the one observed in market samples, that the true proportion of single units with high residue levels was very likely overestimated.

5.4 Linking foods analysed to those consumed

The foods analysed were linked to those recorded in the food consumption database, either via a food conversion model or directly (section 2.6).

Linking of foods is a large source of uncertainty in an exposure assessment, especially when the foods analysed are not those actually

consumed. Residues of PPPs are analysed in raw agricultural commodities (RACs) within monitoring programmes to establish whether commodities comply with maximum residue limits. These analyses are performed as part of different monitoring obligations prescribed in legislation and therefore available every year. However, when using these data, a food conversion model is needed to include all relevant foods consumed (including processed and composite foods) in the assessment. Without this model, only the foods consumed as RAC can be included, resulting in an underestimation of the exposure. So for example, the exposure via apple consumption could be included, but not that via the consumption of apple pie and apple juice.

Advantage of such a model is that concentrations analysed in RACs are linked to consumed amounts of composite foods, which contain these RACs as ingredient, or of processed foods consisting of a single RAC ingredient (e.g. cooked cauliflower, frozen spinach) (section 2.6). These foods are thus included in the assessment without the need to analyse them separately. A disadvantage of this approach is that there is no direct link between analysed and consumed foods. As a result, there is always an uncertainty whether the calculated concentrations in consumed foods via the food conversion model are representative for the concentrations in those actually consumed. The residue database contained some data in foods as consumed (section 2.6). The number of samples was however too limited for fruit juices and some processed cereals. These data were therefore not included in the assessment. The residue levels present in these foods estimated via those analysed in the corresponding RACs and the food conversion model. Increasing the number of analyses of these foods could result in a better estimate of the residue levels in these foods.

An additional uncertainty related to the use of residue levels in RACs and the use of the food conversion model is the change in the composition of food products over time. The food conversion model was generated in 1995 and has since then only been updated by including additional food products recorded in the ensuing food consumption surveys. The composition of the already included food products has not been updated and therefore the composition may no longer be representative for all relevant foods currently on the market. Furthermore, recipes in the conversion table were based on information from cook books, food act, literature, label of the food, internet or manufacturer (van Dooren et al., 1995), resulting in one typical recipe per food. Variations in recipes were not addressed. This was also true for the conversion factors within the conversion model.

Considering these uncertainties, using concentrations analysed in RACs may have resulted in over- or underestimates of the exposure. However, considering the large number of foods included, overall the uncertainties may have levelled out in the final exposure estimates.

5.5 Exposure assessment

The cumulative exposure was performed largely in accordance to the 2012 EFSA guidance on the use of the probabilistic methodology for modelling dietary exposure to residues of PPPs (EFSA, 2012). In this

guidance, the Panel proposes a methodology for performing probabilistic dietary exposure assessment of single and multiple substances of PPPs using two different model runs: an optimistic and a pessimistic model run. In the optimistic model run the major uncertainties are treated using assumptions that are expected to result in underestimates of exposure, whereas in the pessimistic model run these uncertainties are treated in such a way that it is expected to result in overestimates of exposure. Boon et al. (2015) used both model runs to estimate the cumulative acute and chronic exposure to a selected group of residues of PPPs of the triazole group in different European countries. This study showed that the outcomes of the pessimistic model run could be far from reality, especially due to the assumptions regarding the presence of residues of PPPs in animal commodities and disregarding the reducing effect of food handling on residue levels (Boon et al., 2015). The results raised the question for the need of a kind of intermediate 'realistic' scenario combining the optimistic and pessimistic model run in such a way that it results in more realistic estimates of exposures that can still be argued to be conservative (precautionary principle) but not over-conservative.

Such an approach was developed in the FPA study, the 'tier 2 scenario b', that is still deemed conservative, but less than the pessimistic model run. For example, the presence of residues of PPPs in drinking water is still considered for the five most potent substances within a CAG, but at a lower level than in the pessimistic model run: 0.05 µg/L in this report and 0.1 µg/L in the pessimistic model run. In the optimistic model run, exposure via drinking water is assumed to be absent. Another difference is that the presence of residues in animal commodities is only considered when analysed in monitoring programmes. This source of exposure was not included in the current assessment, because residues of PPPs are not analysed in animal commodities in the Dutch monitoring programme. Considering that residue levels in animal commodities are expected to be absent or very low, it is not expected that this has resulted in an underestimation of the exposure.

In this study, the observed individual means (OIM) model was used for assessing the chronic cumulative exposure as recommended in the EFSA guidance (EFSA, 2012) and is the same model as used in the FPA study. Using this model, the distribution of individual mean exposure over the person-days in the food consumption databases is taken as a proxy for the chronic exposure distribution (section 2.11). Given the limited number of person-days in a food consumption database per person, in our case two (Appendix E), and the variation in daily food consumption patterns within an individual, the distribution of mean exposures over individuals obtained using OIM will often be too wide in comparison to distributions of 'true' long term exposures across individuals (Goedhart et al., 2012). This results in exposures that are about right in the middle of the exposure distribution, but are too high in the upper tail and too low in the lower tail of the exposure distribution. Given the high MOEs, refinement of the assessment using more advanced models for assessing the 'true' chronic exposure seems not necessary.

5.6 Cumulative assessment groups (CAGs)

A detailed analysis of the uncertainties concerning the CAGs will be presented in the EFSA scientific report "Establishment of cumulative assessment groups of pesticides for their effects on the nervous system" of which a draft is currently available on the EFSA website for public consultation (EFSA, 2018a). Three important uncertainties related to the CAGs that may have affected the exposure estimates reported here are discussed in more detail below.

In 2013, the EFSA PPR Panel presented a stepwise approach of grouping substances belonging to a CAG (EFSA, 2013). This approach defines four levels of detail of grouping. Starting from a common general target organ or system (CAG level 1), a grouping can be refined based on specific phenomenological effects (CAG level 2), and potentially further based on information about the common mode of action (CAG level 3) and a common mechanism of action (CAG level 4). If a cumulative risk assessment using CAGs defined at a higher level (level 1 or 2) exceeds a threshold of acceptance, refinement of the CAGs (at level 3 or 4) will be an option to obtain a more realistic cumulative exposure estimate. The CAGs addressed in the current report were defined at CAG level 2 (EFSA, 2013). Refinement of the CAG could result in a decrease of the number of substances belonging to the CAG and thus to a lower exposure estimate. This may be the case for substances in the CAG for acute effects on motor division, as well as for those in the two CAGs covering chronic effects on the thyroid. For the CAG covering neurochemical effects, this is unlikely as all of these substances (mostly organophosphate and carbamate insecticides) are included in this CAG based on their potency to inhibit cholinesterase activity, which is the indicator for this CAG.

In the current assessment, all substances belonging to a CAG were assumed to produce the common adverse effect. However, as argued in the draft EFSA report "Establishment of cumulative assessment groups of pesticides for their effects on the nervous system", this may not always be certain based on the underlying toxicity data. It is proposed to include this uncertainty in the risk analysis. In the present study, we did not consider this as clear guidance on this is pending. Furthermore, information on this was not available for the two CAGs covering effects on the thyroid, whereas for the CAGs covering acute effects on the nervous system, this information was only available in the draft report (EFSA, 2018a), and therefore not yet finalised.

Thirdly, it is assumed in the current assessment that the substances belonging to a CAG combine their individual toxicities according to the dose-addition model. The uncertainties concerning this assumption are addressed in the EFSA draft report (EFSA, 2018a). Dose-addition is expected when substances in a mixture act by the same mode of action, and differ only in their potencies. This is the case for the CAG-neurochemical that is based on the inhibition of acetylcholinesterase. For the other three CAGs considered, the modes of action by which the substances exert their effect are often unknown and may differ. It is not clear whether in such a case the dose-addition model applies. As mentioned by EFSA (2018a), a public consultation conducted by EFSA

indicated that this assumption was generally considered as resulting in a possible overestimation of the actual risks.

Finally, the CAGs with an acute effect on the nervous system as proposed in the draft document deviate slightly from the CAGs used in this report (EFSA, 2018a). Generally, these adjustments can result in either lower or higher estimates of the cumulative exposure to both these CAGs. However, the actual impact can only be ascertained by repeating the exposure assessments using the adjusted CAGs.

5.7 Summary uncertainty assessment

The different sources contributing to the uncertainty in the exposure estimates are summarized in Table 4, including the direction and magnitude of the uncertainty relative to the exposure estimate, using the format as proposed by EFSA (2006; 2012). Overall, the cumulative exposure estimates to the four CAGs were likely to be conservative, mainly due to the assumptions about the presence of residues of PPPs in drinking water, the use of monitoring data, and lack of processing information. In addition, the use of CAGs defined at level 2 may have resulted in an overestimation of the exposure for the two CAGs covering effects on the thyroid and the CAG for acute effects on motor division. The cumulative exposure to the two CAGs covering effects on the thyroid was furthermore most likely overestimated at the right tail of the exposure distribution by the use of OIM.

Table 4. Sources, direction and magnitude of uncertainty in the cumulative exposure assessment to the four cumulative assessment groups via food

Source of uncertainty[1]	Direction & Magnitude[2]	Section[3]
Food consumption data		5.1
Food consumption data of 2005-2012	-/•	
Overreporting of fruits and vegetables	+	
Underreporting of body weights for ages 7 to 69	+	
Coding according to FoodEx1	+	
Concentrations		5.2
Representativity samples for consumed foods	+	
Imputation of samples with concentration < LOQ	--/++	
Imputation of samples with missing values[4]	--/++	
Assumed levels in drinking water	+	
30 RACs included	•	
Least potent substance in complex residue definitions (except for CAG-neurochemical and CAG-calcitonin)	--	
Processing factors		5.3
Lack of processing factors	++	
Food mapping		5.4
Via RAC	•	
Exposure model		5.5
Use of OIM for calculating chronic exposure	+	
Cumulative assessment groups (CAGs)		5.6
CAGs defined at level 2 (except for CAG-neurochemical)	++	
Overall assessment: Based on this qualitative evaluation of different uncertainty sources, it was concluded that the cumulative exposure to all CAGs is likely to be conservative due to the assumption of pesticide residues in drinking water, the use of monitoring data and lack of processing factors. In addition, the use of CAGs defined at level 2 may have resulted in an overestimation of the exposure for the two CAGs covering effects on the thyroid and the CAG for acute effects on motor division. The cumulative exposure to the two CAGs covering effects on the thyroid was furthermore most likely overestimated at the right tail of the exposure distribution by the use of OIM.	++	5.7

CAG: cumulative assessment group; LOQ: limit of quantification; OIM: observed individual means; NOAEL: no-observed adverse effect level; RAC: raw agricultural commodity; RPF: relative potency factor

[1] Apart from the listed sources of uncertainty, also the uncertainty due to the sampling size of the concentration and food consumption data was quantified via a bootstrap analysis (section 2.11). This uncertainty was quantified as the 95% confidence interval around the estimated percentiles of exposure (section 2.11).

[2] +, ++, +++ = uncertainty likely to cause small, medium or large overestimation of exposure; -, --, --- = uncertainty likely to cause small, medium or large underestimation of exposure; • = uncertainty likely to cause a negligible effect on exposure estimate

[3] Section in which the uncertainty source is discussed

[4] Only relevant for the acute cumulative assessments

6 Discussion

In this report, the cumulative exposure via food to four cumulative assessment groups (CAGs) of active substances of plant protection products (PPPs) was calculated. These groups of substances were defined by the EFSA PPR panel in 2013 (EFSA, 2013), and updated in 2016 by EFSA as part of the FPA study (section 1). The cumulative exposure reported here was calculated according to the most refined scenario used in the FPA study. Compared to that study, more recent residue concentration relevant for the Dutch market were used in the current study (section 2.4) as well as food consumption data covering, apart from children aged 2 to 6, also older age groups up to 70+ (section 2.5).

Below, the results of the exposure assessment described in this report will be discussed. Also a preliminary interpretation of the possible health risks of the cumulative exposure and its limitations will be discussed.

6.1 Cumulative exposure via food

The margins of exposure (MOEs) of both CAGs regarding chronic effects on the thyroid were much higher than to both CAGs with acute effects on the nervous system (Tables 1, 2 and 3). This observation is in line with exposure assessments to single residues of PPPs, which have also shown that acute health risks related to PPP residue exposure are more likely to occur than chronic health risks (e.g. EFSA, 2015a; 2016).

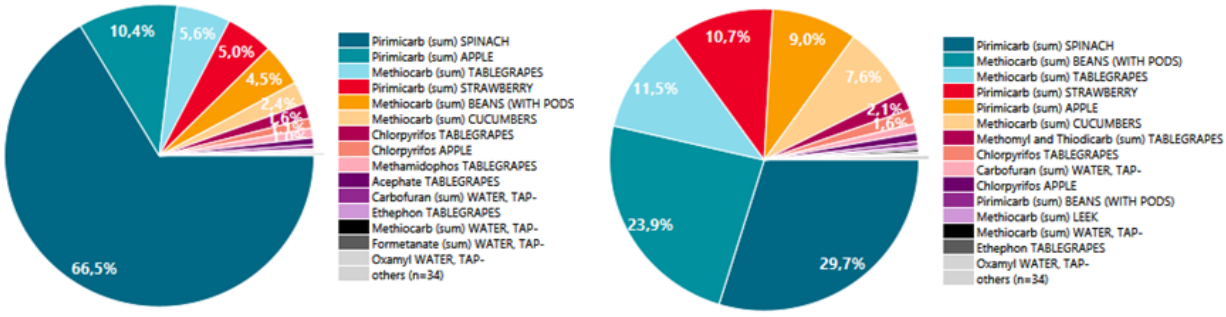
In turn, the MOEs for the CAG covering acute effects on motor division were higher than those for the CAG covering acute neurochemical effects: about three and five times higher at the P99.9 and P99.99 of exposure, respectively (Tables 1 and 2). A larger number of substances within a CAG does therefore not necessarily result in lower MOEs: the CAG-motor division consisted of 64 substances and the CAG-neurochemical of ‘only’ 24 (Appendices A and B). Cumulative exposure depends on the relative potency of the individual substances within a CAG, the residue levels, and amount of foods consumed that may contain these residues. For example, a substance analysed at low levels having a low RPF may still be an important contributor to the exposure when present in highly consumed foods. Given the large number of substances and foods involved in a cumulative exposure assessment, it is hard to predict the outcome without performing these assessments. Furthermore, the MOEs of both CAGs were roughly 2.5-fold higher in young children compared to the older age groups (Tables 1 and 2). This difference can be explained by a higher consumption level per kg body weight in this age group.

Cumulative exposure can occur either via the consumption of different foods which contain different residues of PPPs and/or via more than one residue in a food product. Examining the samples with a positive concentration for at least one substance of the CAG-neurochemical (n=485) showed that 458 samples (94%) were positive for one substance, 26 (5%) for two substances and one (0.2%) for three

substances. The most prevalent combinations were chlorpyrifos together with another organophosphate pesticide and acephate with methamidophos. The commodities containing two substances were mainly oranges (n=11), mandarins (n=4) and table grapes (n=3). For the CAG-motor division, 1103 (71%) samples with a positive concentration for at least one substance belonging to this CAG were positive for one substance. The numbers for two, three, four and five substances were 347 (22%), 94 (6%), 25 (2%) and 7 (0.4%). For this CAG, the number of possible combinations was very diverse due to the large number of substances included. The exposure to both CAGs was therefore more a result of the consumption of different foods containing different substances than of single foods containing a mixture of substances. Cumulative assessments should therefore always include all foods that may contain the substances of a CAG.

Important contributors to the cumulative exposure
As the exposure to the CAG-neurochemical seemed most critical, as reflected in lower MOEs (section 3), the important contributors to the exposure in the right tail of the exposure distribution of this CAG were examined in more detail. In all age groups, the exposure in that part of the distribution was largely determined by the presence of pirimicarb in spinach, followed by methiocarb in beans (with pod) in the older three age groups and pirimicarb in apple in young children (section 4.1.1). Figure 1 shows the contributions for children aged 2 to 6 and 7 to 17 (see Appendix S for the other two age groups).

Pirimicarb was detected at a level above the limit of quantification (LOQ) in two spinach samples out of 87 analysed. For apple, 17 samples were positive for pirimicarb out of 147 analysed. The levels detected for spinach and apple (maximally 0.68 and 0.088 mg/kg, respectively) were all well below the MRL of 2 mg/kg that was in force during the majority of the period covered in this study (2014-2016). From 16 August 2016, the MRLs have been changed to 0.06 mg/kg for spinach and 0.5 mg/kg



2 to 6 years 7 to 17 years

Figure 1. Contribution of substance/commodity combinations to the upper 0.1% of the acute cumulative exposure distribution of CAG-neurochemical for children aged 2 to 6 and 7 to 17. For the two other age groups, see Appendix S.

for apple[16]. Considering these new MRLs, both levels of pirimicarb in spinach exceeded the MRL, whereas for apple still no exceedances were observed. These spinach and apple samples contained no other substances belonging to the CAG-neurochemical. Examining the nine exposures around the P99.9 in children aged 2 to 6[17] showed that the contribution of spinach to this exposure level was solely related to the consumption of frozen spinach. Consumption levels ranged from 28 to 48 grams per day. For apple, only one exposure was simulated around the P99.9 based on an apple consumption level of 86 grams. These results show that the exposure to CAG-neurochemical at the right tail of the exposure distribution is not due to extreme high consumption levels, but due to a combination of both consumption and residues analysed.

For the three older age groups, the presence of methiocarb in beans (with pods) was also an important contributor to the exposure to the CAG-neurochemical (section 4.1.1). Methiocarb was present at a level above LOQ in two out of 256 bean samples analysed. The two levels were well below the MRL (0.2 mg/kg): maximally 0.085 mg/kg. One of the positive bean samples contained also pirimicarb. The consumption of these beans (in grams per day) was higher in the three older age groups compared to young children, explaining the difference in contribution of this food to the cumulative exposure to CAG-neurochemical between the age groups: 24-25% compared to 5% (Appendix S). For methiocarb in beans (with pod), the current MRL is still 0.2 mg/kg.

Given the reduction of the MRL of pirimicarb in spinach from 16 August 2016 onwards, the exposure to the CAG-neurochemical is likely to decrease. Additional options to lower the exposure to this CAG, if warranted, could be to investigate if the use of pirimicarb in both spinach and apple, and that of methiocarb in beans (with pods) could be replaced by less potent substances within the same CAG or by a substance that is not part of the CAG-neurochemical. Especially, methiocarb, with an RPF of 2, was one of the two second most potent substances in the CAG-neurochemical (Appendix A). Only carbofuran with an RPF of 6.67 was more potent.

Contribution of strawberry to the exposure
Cumulative exposure is relevant for substances that have the same toxic effect in tissues, organs and physiological systems (EFSA, 2013). Substances that do not belong to such groups of substances can only be evaluated individually; until they may be included in the CAGs still to be defined for remaining organs, tissues and physiological systems. Presently, four CAGs have been defined and were included in this report.

The reason for this study was the observation in 2017 that strawberry samples can contain multiple residues of PPPs (section 1). In the cumulative exposure assessment, strawberry contributed however less than 10% to the upper 0.1% of the cumulative exposure distribution in all age groups for the CAGs covering acute effects on the nervous system, except for children aged 7 to 17 for the CAG-neurochemical. In

[16] Commission Regulation (EU) 2016/71
[17] Via the drill-down option within MCRA

this age group and CAG, strawberry contributed for 11% to the upper 0.1% of the exposure distribution (section 4.1.1).

Also the monitoring results included in this study showed that strawberry can contain different residues of PPPs. In total, 163 strawberry samples were analysed of which 87% (n=142) contained multiple substances at levels above the LOQ. The number of strawberry samples with 2 to 5, 5 to 10, 11 to 15, and more than 15 substances at a level above LOQ was 64, 84, 13 and 1, respectively. The highest number of substances analysed in one sample was 19, which was the case for one strawberry sample. Despite this, strawberry was not a major contributor to the cumulative exposure to CAGs regarding acute effects on the nervous system, because the majority of the substances did not belong to these CAGs. For example, the strawberry sample with 19 substances contained only one substance of the CAG-neurochemical (pirimicarb) and one of the CAG-motor division (fluopyram).

The majority (96%) of the other substances detected at levels above the LOQ was present at levels below the MRL. In six strawberry samples, exceedances of the MRL were detected for one substance; in one sample even for two substances. In the five samples with one exceedance of the MRL, two referred to a substance that belonged to the CAG-thyroid hormone (mepanipyrim and spinosad) and were therefore included in the cumulative exposure estimate to this CAG. This was also true for one of the substances (spinosad) in the strawberry sample with two exceedances of the MRL. The remaining exceedances (n=4) related to the presence of trifloxystrobin (n=3) and spiroxamine (n=1). Trifloxystrobin is a substance for which acute toxicity is not relevant[18]. A chronic health risk due to the consumption of strawberry that may contain this substance at the detected high levels is considered as very low, because the majority of the strawberry samples contained this substance at levels below the MRL. For a chronic health risk, a long-run average exposure is relevant; an incidental high exposure will thus be compensated with many low exposures and no exposures on days that no strawberry is consumed or the strawberry does not contain the residue. For spiroxamine, however, acute toxicity has been established. Therefore, a single substance risk assessment should be conducted to determine if acute health risks can be excluded when consuming large portions of strawberry containing residues of spiroxamine at the level detected. Using version 3 of PRIMo (EFSA, 2018b) showed that the exposure to spiroxamine via strawberry was maximally 2% of the acute reference dose (0.1 mg/kg bw[16]) in children indicating that the health risk is negligible[19].

6.2 Risk characterisation

In this report, the margin of exposure (MOE) was used for the purpose of risk characterisation (section 3). There is presently no guidance on

[18] http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.detail&language=EN&selectedID=1991

[19] In this assessment, a conversion factor of 2.3 (for wine grapes) was used to convert the residue definition for enforcement and monitoring of spiroxamine to that for risk assessment (EFSA, 2015b). There is no specific conversion factor available for strawberry. Therefore, the highest factor available for fruit crops was used.

the evaluation of the cumulative exposure regarding possible health risks.

To characterize the risk related to the exposure to groups of substances based on the MOE approach, two decisions are needed. First, the relevant exposure percentile of the exposure distribution for the calculation of the MOE needs to be determined. The Environmental Protection Agency of the United States (US EPA) uses the P99.9 of the exposure distribution as a reference point when considering the acute exposure (US EPA, 2000; 2006). This means that if the exposure at the P99.9 is below the health-based guidance value, the health risk is considered negligible. In the past, due to the absence of guidance at the European level, this exposure level was used for assessing possible risks related to the acute exposure to groups of residues of PPPs in different studies (Blaznik et al., 2015; Boon et al., 2008; 2012; Jensen et al., 2009).

The MOE quantifies the margin between a 'safe intake level' and the exposure (section 3). To establish if there is a health risk based on a MOE, also the minimum level of the MOE for a negligible health risk should be established.

Which reference point of the cumulative exposure distribution to use and what the minimal MOE should be for a cumulative risk assessment are risk management decisions, which are not within the mandate of the risk assessor. For the EU, this has to be decided by the European Commission.

Fenbuconazole and ioxynil were the index compounds of the CAG-calcitonin and CAG-thyroid hormone, respectively. If the criteria for the minimum value of the MOE for both index compounds as applicable for a single substance assessment were used, the minimal value would be 100 (EFSA, 2010a; b). As the MOEs of these CAGs far exceeded this minimum value, even at the P99.99 level of exposure, it could be concluded that the occurrence of adverse health effects due to chronic exposure to both CAGs are not expected in the Netherlands.

Oxamyl was the index compound of the two CAGs covering acute effects on the nervous system. If also here the criteria for the minimum value of the MOE for oxamyl as for a single substance assessment were applied, the minimal value would be again 100 (EFSA, 2005a). Based on the P99.9 of exposure and this minimum value, the best estimates of MOEs reported here were at least 116 for the CAG-neurochemical and 415 for the CAG-motor division (Tables 1 and 2). Thus, based on these assumptions, it could be concluded that the risk of adverse health effects due to the cumulative exposure to the two CAGs are not to be expected for the CAG-motor division. For the CAG-neurochemical, the MOE at the P99.9 was however close to 100 and a risk could therefore not be excluded. Additionally, it is noted that when the lower confidence limit of the MOE is taken into account, the MOE of the CAG-neurochemical would be lower than 100 for children aged 2 to 6 and slightly lower in persons aged 70+ (Table 1). This means that considering the uncertainty due to the limited size of the food consumption and concentration databases that there is a probability that

the real MOE may also be lower than 100, especially in young children, but with equal probability also higher.

If the P99.99 of exposure had been selected for risk characterisation purposes, the MOEs would have been less than 100 for the CAG-neurochemical in young children (Table 1) and persons age 70+ and would still have been higher than 100 for the CAG-motor division (Table 2). The conclusions about possible health risks would have been the same for both CAGs as with the P99.9.

7 Conclusion

Based on a preliminary risk assessment, with the assumptions on the percentile of exposure (P99.9) and the minimal margin of exposure relevant for risk management (100) as described in section 6.2, the exposure to three CAGs is not expected to result in adverse health effects in the Netherlands due to MOEs that largely exceeded 100 at the P99.9 of exposure for all age groups. For the CAG-neurochemical, the MOE at the P99.9 of exposure for children aged 2 to 6 was close to 100 and a possible health risk could therefore not be excluded. It should be noted that the exposure estimates very likely overestimate the real exposure, due to the assumptions made and input data used in the assessment (Table 4). Furthermore, the MRLs of pirimicarb in spinach and apple, two combinations that contributed largely to the exposure to the CAG-neurochemical in children aged 2 to 6, were lowered in 2016. Due to this, the exposure to this CAG is likely to decrease.

Strawberry was not an important source of cumulative exposure to the CAGs examined. Strawberry can contain multiple substances. However, as the majority of these substances do not belong to one of the four CAGs addressed, the product was not an important source of exposure to any of the CAGs.

Currently, the evaluation of cumulative exposure estimates is under discussion at EFSA. This discussion includes the composition of the CAGs, how to include the uncertainty in the toxicity data of the active substances (and thus their relevance for inclusion in the CAG) and those in the exposure assessment, and how to evaluate the cumulative exposure estimates in relation to possible health risks. In addition, a decision on the minimal MOE for negligible health at which reference point of the exposure distribution is required for the performance of a risk characterisation. This decision is up to the European Commission. When all of this becomes clear, the cumulative exposure estimates presented in this report may need to be re-evaluated to determine if the preliminary conclusion of no health risk remains valid.

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List of abbreviations

ADI	acceptable daily intake
ARfD	acute reference dose
BfR	German Federal Institute for Risk Assessment
BMDL	lower limit of the benchmark dose
bw	body weight
CAG	cumulative assessment group
DNFCS	Dutch National Food Consumption Survey
EC	European Commission
EFSA	European Food Safety Authority
EPA	Environmental Protection Agency
EU	European Union
EUCP	EU-coordinated programme
FPA	Framework Partnership Agreement
GAP	good agricultural practice
HBGV	heath-based guidance value
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
LOQ	limit of quantification
OIM	observed individual means
MCRA	Monte Carlo Risk Assessment
MOE	margin of exposure
MRL	maximum residue limit
NOAEL	no-observed adverse effect level
PPP	plant protection product
PPR	Plant Protection Product and their Residues
PRIMo	Pesticide Residue Intake Model
RAC	raw agricultural commodity
RASFF	Rapid Alert System for Food and Feed (RASFF)
RD	residue definition
RPF	relative potency factor
SSD	Standard Sample Description
TDS	Total diet study
US	United States

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Appendix A. Overview of the substances belonging to the cumulative assessment group (CAG) for acute neurochemical effects, as well as their no-observed adverse effect levels (NOAELs) and relative potency factors (RPFs)

Substance		NOAEL	
Code	Name	(mg/kg bw)	RPF
RF-0065-001-PPP	Carbofuran	0.015	6.67
RF-0020-001-PPP	Aldicarb	0.05	2
RF-0291-001-PPP	Methiocarb	0.05	2
RF-0223-001-PPP	Formetanate	0.1	1
RF-0320-001-PPP	**Oxamyl**[1]	**0.1**	**1**
RF-0347-001-PPP	Pirimicarb	0.2	0.5
RF-0068-001-PPP	Methamidophos	0.3	0.333
RF-0293-001-PPP	Methomyl[2]	0.25	0.4
RF-0139-001-PPP	Omethoate[3]	0.25	0.4
RF-0226-001-PPP	Carbosulfan	0.5	0.2
RF-0187-001-PPP	Chlorpyrifos	0.5	0.2
RF-0293-001-PPP	Ethoprophos	0.5	0.2
RF-0351-001-PPP	Fosthiazate	0.5	0.2
RF-0139-001-PPP	Profenofos	0.5	0.2
RF-0164-001-PPP	Thiodicarb[2]	0.5	0.2
RF-0293-001-PPP	Dimethoate[3]	1	0.1
RF-0033-001-PPP	Fenthion	1	0.1
RF-0012-001-PPP	Azinphos-methyl	2	0.05
RF-0123-001-PPP	Acephate	2.5	0.04
RF-0173-001-PPP	Diazinon	2.5	0.04
RF-0338-001-PPP	Fenamiphos	2.7	0.037
RF-0266-001-PPP	Phosmet	4.5	0.0222
RF-0435-001-PPP	Malathion	10	0.01
RF-0348-001-PPP	Trichlorfon	10	0.01
RF-0160-001-PPP	Pirimiphos-methyl	15	0.0067
RF-0065-001-PPP	Ethephon	22	0.0045

bw: body weight; CAG: cumulative assessment group; NOAEL: no-observed adverse effect level; RD: residue definition; RPF: relative potency factor

[1] Index compound

[2] The residue data for these two substances are reported in the monitoring as methomyl (RD) with residue definition (RD) 'methomyl and thiodicarb (sum of methomyl and thiodicarb expressed as methomyl)'. Methomyl is approved and thiodicarb is not. In the cumulative assessment, the concentrations of methomyl (RD) were assumed to relate to the presence of thiodicarb (less potent).

[3] The residue data for these two substances are reported in the monitoring as dimethoate (RD) with RD 'sum of dimethoate and omethoate expressed as dimethoate'. Dimethoate is approved and omethoate is not. In the cumulative assessment, the concentrations of dimethoate (RD) were assumed to relate to the presence of dimethoate (less potent).

Appendix B. Overview of the substances belonging to the cumulative assessment group (CAG) for acute functional effects on the motor division, as well as their no-observed adverse effect levels (NOAELs) and relative potency factors (RPFs)

Substance		NOAEL	
Code	Name	(mg/kg bw)	RPF
RF-0020-001-PPP	Aldicarb	0.05	2
RF-0320-001-PPP	**Oxamyl**[1]	**0.1**	**1**
RF-0291-001-PPP	Methiocarb	0.25	0.4
RF-0139-001-PPP	Omethoate[2]	0.35	0.29
RF-0213-001-PPP	Fluquinconazole	0.45	0.222
RF-0192-001-PPP	Fipronil	0.5	0.2
RF-0164-001-PPP	Thiodicarb[3]	0.5	0.2
RF-0261-001-PPP	Lambda-Cyhalothrin	0.52	0.192
RF-0293-001-PPP	Methomyl[3]	0.75	0.133
RF-0108-001-PPP	Cyfluthrin, beta-[4]	0.5	0.2
RF-0108-001-PPP	Cyfluthrin[4]	1	0.1
RF-0018-001-PPP	Acrinathrin	1	0.1
RF-0112-001-PPP	Cypermethrin, beta-[5]	1	0.1
RF-0120-001-PPP	Deltamethrin	1	0.1
RF-0021-001-PPP	Dieldrin[6]	1	0.1
RF-0187-001-PPP	Fenthion	1	0.1
RF-0223-001-PPP	Formetanate	1	0.1
RF-0289-001-PPP	Methamidophos	1	0.1
RF-0068-001-PPP	Carbosulfan	1.2	0.083
RF-0010-001-PPP	2,4-D	1.5	0.067
RF-0011-001-PPP	Abamectin	1.5	0.067
RF-0451-001-PPP	Ziram[7]	1.5	0.067
RF-0173-001-PPP	Fenamiphos	1.52	0.066
RF-0690-004-PPP	Esfenvalerate[8]	1.8	0.056
RF-0033-001-PPP	Azinphos-methyl	2	0.05
RF-0040-001-PPP	Benfuracarb	2	0.05
RF-0323-001-PPP	Oxydemeton-methyl	2	0.05
RF-0428-001-PPP	Triadimefon[9]	2	0.05
RF-0112-001-PPP	Cypermethrin, alpha-[5]	2.3	0.043
RF-0155-001-PPP	Endosulfan	3	0.033
RF-0263-001-PPP	Lindane	3	0.033
RF-0417-001-PPP	Thiacloprid	3.1	0.032
RF-0164-001-PPP	Ethoprophos	5	0.02
RF-0408-001-PPP	Tefluthrin	5	0.02
RF-0151-001-PPP	Thiram[7]	5	0.02

Substance		NOAEL	
Code	Name	(mg/kg bw)	RPF
RF-0226-001-PPP	Fosthiazate	5.4	0.019
RF-0112-001-PPP	Cypermethrin[5]	7.5	0.013
RF-0203-001-PPP	Flufenacet	7.5	0.013
RF-0282-001-PPP	Metaldehyde	7.5	0.013
-	Sulfoxaflor	7.5	0.013
RF-0338-001-PPP	Phosmet	9	0.011
RF-0014-001-PPP	Acetamiprid	10	0.01
RF-0112-001-PPP	Cypermethrin, zeta-[5]	10	0.01
RF-0183-001-PPP	Fenpropathrin	10	0.01
RF-0303-001-PPP	Milbemectin	10	0.01
RF-0347-001-PPP	Pirimicarb	10	0.01
RF-0403-001-PPP	Tebuconazole	10	0.01
RF-0435-001-PPP	Trichlorfon	10	0.01
RF-0180-001-PPP	Fenitrothion	12.5	0.008
RF-0130-001-PPP	Dicofol	15	0.007
RF-0139-001-PPP	Dimethoate[2]	20	0.005
RF-0139-001-PPP	Pyrethrins	20	0.005
RF-0374-001-PPP	Pyridate	20	0.005
RF-0376-001-PPP	Imidacloprid	23.5	0.004
RF-0250-001-PPP	Bifenthrin	35	0.003
RF-0046-001-PPP	Dicamba	30	0.003
RF-0124-001-PPP	Tetraconazole	30	0.003
RF-0414-001-PPP	Tri-allate	36	0.003
RF-0430-001-PPP	Chlorpropham	50	0.002
RF-0086-001-PPP	Clothianidin	60	0.002
RF-0690-001-PPP	Fenvalerate[8]	56	0.002
RF-1071-001-PPP	Fluopyram	50	0.002
RF-0251-001-PPP	Indoxacarb	50	0.002
RF-0275-001-PPP	Mepiquat	58	0.002
RF-0633-001-PPP	Penflufen	50	0.002
RF-0232-001-PPP	Dinotefuran	100	0.001
RF-0348-001-PPP	Glufosinate	100	0.001
RF-0396-001-PPP	Pirimiphos-methyl	150	0.001
RF-0409-001-PPP	Spirotetramat	100	0.001
RF-0418-002-PPP	Tembotrione	200	0.001
RF-0842-001-PPP	Thiamethoxam[10]	100	0.001
RF-0633-001-PPP	Permethrin	750	0.0001

bw: body weight; CAG: cumulative assessment group; NOAEL: no-observed adverse effect level; RD: residue definition; RPF: relative potency factor

[1] Index compound

[2] The residue data for these two substances are reported in the monitoring as dimethoate (RD) with residue definition (RD) 'sum of dimethoate and omethoate expressed as dimethoate'. Dimethoate is approved and omethoate is not. In the cumulative assessment, the concentrations of dimethoate (RD) were assumed to relate to the presence of dimethoate (less potent).

[3] The residue data for these two substances are reported in the monitoring as methomyl (RD) with RD 'methomyl and thiodicarb (sum of methomyl and thiodicarb expressed as

methomyl)'. Methomyl is approved and thiodicarb is not. In the cumulative assessment, the concentrations of methomyl (RD) were assumed to relate to the presence of methomyl (less potent).
[4] The residue data for these two substances are reported in the monitoring as cyfluthrin (RD) with RD 'cyfluthrin including other mixtures of constituent isomers (sum of isomers)'. Cyfluthrin is not approved and beta-cyfluthrin is. In the cumulative assessment, the concentrations of cyfluthrin (RD) were assumed to be related to the presence of cyflutrhin (less potent). As cyflutrhin is not approved, concentrations related to cyfluthrin (RD) were assumed to be zero.
[5] The residue data for these substances are reported in the monitoring as cypermethrin (RD) with RD 'cypermethrin including other mixtures of constituent isomers (sum of isomers). In the cumulative assessment, concentrations of cypermethrin (RD) were assumed to be related to the presence of zeta-cypermethrin (least potent).
[6] The residue data of dieldrin are reported in the monitoring as dieldrin (RD)' with RD 'aldrin and dieldrin (aldrin and dieldrin combined expressed as dieldrin)'. Both active substances are not approved, and aldrin is not part of the CAG-motor division. In the cumulative assessment, the concentrations of dieldrin (D) were assumed to relate to the presence of dieldrin.
[7] Ziram and thiram belong to the dithiocarbamates. RD of this group is 'dithiocarbamates (dithiocarbamates expressed as CS_2, including maneb, mancozeb, metiram, propineb, thiram and ziram)'. Per commodity, the less potent approved dithiocarbamate (considering all) was established. In case of thiram or ziram, the concentrations were assumed to refer to the less potent. Otherwise, the data were set to zero. Note that no quantifiable concentrations of dithiocarbamates were present in the residue database (Appendix H).
[8] The residue data for these substances are reported in the monitoring as fenvalerate (RD). Esfenvalerate is approved and fenvalerate is not. In the cumulative assessment, the concentrations of fenvalerate (RD) were assumed to be related to the presence of fenvalerate (less potent).
[9] The residue data of triadimefon are reported in the monitoring as triadimefon (RD) with RD 'triadimefon and triadimenol (sum of triadimefon and triadimenol)'. Triadimenol is approved and triadimefon is not. As triadimefon degrades to triadimenol, the concentrations of triadimefon (RD) were assumed to relate to the presence of triadimenol in the cumulative assessment. As triadimenol is not part of the CAG-motor division, the concentrations were assumed to be zero.
[10] The residue data of thiamethoxam are reported in the monitoring as thiamethoxam (RD) with RD 'thiametoxam (sum of thiametoxam and clothianidin expressed as thiametoxam'. In the cumulative assessment, it was assumed that the concentrations related to the presence of thiamethoxam, because clothianidin has a separate RD.

Appendix C. Overview of the substances belonging to the cumulative assessment group (CAG) for chronic effects on parafollicular (C-)cells or the calcitonin system of the thyroid, as well as their no-observed adverse effect levels (NOAELs) and relative potency factors (RPFs)

Substance		NOAEL (mg/kg bw)	RPF
Code	Name		
RF-0065-001-PPP	Carbofuran	0.046	65.22
RF-0126-001-PPP	Dichlorprop-P[1]	0.35	8.57
RF-0351-001-PPP	Profenofos	0.56	5.36
RF-0253-001-PPP	Ioxynil	0.6	5
RF-0254-001-PPP	Ipconazole	1.5	2
RF-0172-001-PPP	Fenamidone	2.8	1.07
RF-0176-001-PPP	**Fenbuconazole**[2]	**3**	**1**
RF-0121-001-PPP	Desmedipham	3.18	0.94
	Ziram[3]	7.7	0.39
RF-0056-001-PPP	Buprofezin	8.7	0.34
RF-1056-001-PPP	Bixafen	12.9	0.23
RF-0154-001-PPP	Dodine	20	0.15
RF-0242-001-PPP	Hexythiazox	29.3	0.1
RF-0250-001-PPP	Imidacloprid	51.3	0.06
RF-0221-001-PPP	Folpet[4]	1800	0.002

bw: body weight; CAG: cumulative assessment group; NOAEL: no-observed adverse effect level; RD: residue definition; RPF: relative potency factor

[1] The residue data of dichlorprop-P are reported in the monitoring as dichlorprop (RD) with residue definition (RD) 'dichloprop (sum of dichlorprop (including dichlorprop-P) and its conjugates, expressed as dichlorprop)'. Dichlorprop-P is approved and dichlorprop is not. In the cumulative assessment, the concentrations of dichlorprop (RD) were assumed to relate to the presence of dichlorprop-P.

[2] Index compound

[3] Ziram belongs to the dithiocarbamates. The residue definition of this group of substances is 'dithiocarbamates (dithiocarbamates expressed as CS_2, including maneb, mancozeb, metiram, propineb, thiram and ziram)'. Per commodity, the less potent approved dithiocarbamate (considering all) was established. In case of ziram, the concentrations were assumed to refer to the presence of ziram. Note that no quantifiable concentrations of dithiocarbamates were present in the residue database.

[4] For the commodities apple, pear, beans (with pods), tomato and strawberry, the residue data of folpet are reported in the monitoring as folpet (RD) with RD 'the sum of captan and folpet'. Both captan and folpet are approved. In cumulative assessment, the concentrations of folpet (RD) were assumed to be related to the presence of captan and subsequently set to zero as captan does not belong to the CAG-calcitonin.

Appendix D. Overview of the substances belonging to the cumulative assessment group (CAG) for chronic effects on follicular cells and/or the thyroid hormone (T3/T4) system, as well as their no-observed adverse effect levels (NOAELs) and relative potency factors (RPFs)

Active substance		NOAEL (mg/kg bw)	RPF
Code	Name		
RF-0253-001-PPP	**Ioxynil**[1]	**0.02**	**1**
RF-0192-001-PPP	Fipronil	0.06	0.33
RF-0130-001-PPP	Dicofol	0.07	0.29
RF-0151-001-PPP	Propineb[2]	0.18	0.11
RF-0383-001-PPP	Quintozene	0.2	0.1
RF-0274-001-PPP	Mepanipyrim	0.245	0.08
RF-0025-001-PPP	Amitrole (aminotriazole)	0.3	0.07
RF-0213-001-PPP	Fluquinconazole	0.44	0.05
RF-0265-001-PPP	Lufenuron	0.4	0.05
RF-0426-001-PPP	Topramezone	0.4	0.05
RF-0151-001-PPP	Metiram[2]	0.5	0.04
RF-0151-001-PPP	Ziram[2]	0.56	0.04pi
RF-0223-001-PPP	Formetanate	0.5	0.04
RF-0300-001-PPP	Metribuzin	0.5	0.04
RF-0075-001-PPP	Chlordane	0.6	0.03
RF-0098-001-PPP	Clofentezine	0.58	0.03
RF-0374-001-PPP	Pyrethrins	0.66	0.03
RF-0409-001-PPP	Tembotrione	0.79	0.03
RF-0010-001-PPP	2,4-D	1	0.02
RF-0056-001-PPP	Buprofezin	0.9	0.02
RF-0118-001-PPP	Dazomet[3]	1	0.02
RF-0168-001-PPP	Ethofenprox	1.1	0.02
RF-1071-001-PPP	Fluopyram	1.2	0.02
RF-0271-004-PPP	MCPA (metabolite of MCPB)[4]	0.95	0.02
RF-0365-001-PPP	Proquinazid	1.2	0.02
RF-0384-003-PPP	Quizalofop-P-tefuryl[5]	1.3	0.02
RF-0414-001-PPP	Tetraconazole	1	0.02
RF-0417-001-PPP	Thiacloprid	1.2	0.02
RF-0017-001-PPP	Aclonifen	3.6	0.01
RF-0040-001-PPP	Benfuracarb	1.63	0.01
RF-1056-001-PPP	Bixafen	2.8	0.01
RF-0055-001-PPP	Bupirimate	3	0.01
RF-0068-001-PPP	Carbosulfan	3.1	0.01

Active substance		NOAEL (mg/kg bw)	RPF
Code	Name		
RF-0114-001-PPP	Cyprodinil	3.14	0.01
RF-0121-001-PPP	Desmedipham	3.18	0.01
RF-0151-001-PPP	Mancozeb[2]	4	0.01
RF-0151-001-PPP	Maneb[2]	3.7	0.01
RF-0172-001-PPP	Fenamidone	3.6	0.01
RF-0199-001-PPP	Flubendiamide	2	0.01
RF-0211-001-PPP	Fluoxastrobin	1.5	0.01
RF-00000024-PAR	Fluxapyroxad	2.7	0.01
RF-0227-001-PPP	Fuberidazole	3.6	0.01
RF-0235-001-PPP	Haloxyfop-P (Haloxyfop-R)[6]	2	0.01
RF-0259-001-PPP	Isoxaflutole	2	0.01
RF-0317-001-PPP	Oxadiargyl	2.1	0.01
RF-0324-001-PPP	Oxyfluorfen	1.94	0.01
RF-0342-001-PPP	Phoxim	4	0.01
RF-0344-001-PPP	Picolinafen	1.7	0.01
RF-0356-001-PPP	Propaquizafop	3	0.01
RF-0369-001-PPP	Pymetrozine	3	0.01
RF-0886-001-PPP	Quinoclamine	2.9	0.01
RF-0393-001-PPP	Spinosad	2.7	0.01
-	Cyantraniliprole	1.4	0.01
RF-00002610-PAR	Fenpyrazamine	4.25	0.005
RF-0039-001-PPP	Benfluralin	5.4	0.004
RF-0086-001-PPP	Chlorprofam	5	0.004
RF-0170-001-PPP	Etridiazole	5	0.004
RF-0176-001-PPP	Fenbuconazole	5.7	0.004
RF-0250-001-PPP	Imidacloprid	5.7	0.004
RF-0315-001-PPP	Orthosulfamuron	5	0.004
RF-0450-001-PPP	Vinclozolin	4.9	0.004
RF-0054-001-PPP	Bromuconazole	6.48	0.003
RF-0129-001-PPP	Dicloran	7.5	0.003
RF-0150-001-PPP	Dithianon	7.9	0.003
RF-0395-001-PPP	Spiromesifen	6.5	0.003
RF-0413-001-PPP	Terbuthylazine	6.97	0.003
RF-0422-001-PPP	Thiophanate-methyl	8	0.003
RF-1057-001-PPP	Valifenalate (formerly valiphenal)	7	0.003
RF-00002607-PAR	8-Hydroxyquinoline (incl. Oxyquinoleine)	10	0.002
RF-1055-001-PPP	Ametoctradin	12.33	0.002
RF-0475-001-PPP	Anthraquinone	12.58	0.002
RF-0043-001-PPP	Benthiavalicarb	9.9	0.002
RF-0062-001-PPP	Carbaryl	10	0.002
RF-0069-001-PPP	Carboxin	12	0.002

Active substance		NOAEL (mg/kg bw)	RPF
Code	Name		
RF-0097-001-PPP	Clodinafop	10.2	0.002
RF-0143-001-PPP	Dinocap	10	0.002
RF-0182-001-PPP	Fenoxycarb	10.1	0.002
RF-00000025-PAR	Isopyrazam	8.3	0.002
RF-0276-001-PPP	Meptyldinocap	11.4	0.002
RF-0118-001-PPP	Metam (incl. - potassium and - sodium)[3]	13.03	0.002
-	Penflufen	9.5	0.002
RF-0364-001-PPP	Propyzamide	8.5	0.002
RF-0876-001-PPP	Pyridalyl	13.3	0.002
RF-0385-001-PPP	Resmethrin[7]	10	0.002
-	Sedaxane	11	0.002
RF-0392-001-PPP	Spinetoram	10	0.002
RF-0416-001-PPP	Thiabendazole	10	0.002
RF-0022-001-PPP	Amidosulfuron	23.7	0.001
RF-0030-001-PPP	Azadirachtin	36	0.001
RF-0037-001-PPP	Beflubatamid	17.7	0.001
RF-0038-001-PPP	Benalaxyl-M[8]	30.1	0.001
RF-0049-001-PPP	Boscalid	22	0.001
RF-0050-001-PPP	Bromide ion	27	0.001
RF-0052-001-PPP	Bromopropylate	26	0.001
RF-0053-001-PPP	Bromoxynil	39.4	0.001
RF-0064-001-PPP	Carbetamide	20.1	0.001
RF-0107-001-PPP	Cyflufenamid	20	0.001
RF-00002591-PAR	Cyflumetofen	39.7	0.001
RF-0113-001-PPP	Cyproconazole	24.7	0.001
RF-0174-001-PPP	Fenamirol	19	0.001
RF-0203-001-PPP	Flufenacet	26.8	0.001
RF-0206-001-PPP	Flumioxazin	19.3	0.001
RF-0208-001-PPP	Fluopicolide	32	0.001
RF-0219-001-PPP	Flutolanil	37	0.001
RF-0262-001-PPP	Lenacil	22.5	0.001
RF-0268-001-PPP	Mandipropamid	21.8	0.001
RF-0308-001-PPP	Myclobutanil	15	0.001
RF-0316-001-PPP	Oryzalin	36	0.001
RF-0318-001-PPP	Oxadiazon	17.8	0.001
RF-00002609-PAR	Penthiopyrad	37.8	0.001
RF-0333-001-PPP	Pethoxamid	17	0.001
RF-0349-001-PPP	Prochloraz	25	0.001
RF-0377-001-PPP	Pyrimethanil	17	0.001
RF-0394-001-PPP	Spirodiclofen	19.88	0.001
RF-0411-001-PPP	Tepraloxydim	14	0.001
RF-0425-001-PPP	Tolylfluanid	33	0.001

Active substance		NOAEL (mg/kg bw)	RPF
Code	Name		
RF-0428-001-PPP	Triadimefon[9]	15	0.001
RF-0950-001-PPP	Tribenuron (aka metometurun)	15	0.001
RF-0442-001-PPP	Trifluralin	30	0.001
RF-0132-001-PPP	Diethofencarb	42.7	0.0005
RF-0331-001-PPP	Pendimethalin	43	0.0005
RF-0106-001-PPP	Cycloxydim	50	0.0004
RF-0346-001-PPP	Pinoxaden	50	0.0004
RF-0389-001-PPP	Silthiofam	50.5	0.0004
RF-0096-001-PPP	Clethodim[10]	62	0.0003
RF-0221-001-PPP	Folpet[11]	68.4	0.0003
RF-0249-001-PPP	Imazosulfuron	75	0.0003
RF-0267-001-PPP	Maleic hydrazide	63	0.0003
-	Pyriofenone	61.6	0.0003
-	Sulfoxaflor	79.4	0.0003
RF-0470-001-PPP	Amisulbrom	129	0.0002
RF-0038-001-PPP	Benalaxyl[8]	100	0.0002
RF-0048-001-PPP	Bitertanol	100	0.0002
RF-0245-001-PPP	Hymexazol	98	0.0002
RF-0448-001-PPP	Tritosulfuron	92	0.0002
RF-0418-002-PPP	Thiamethoxam[12]	198.6	0.0001
RF-00002593-PAR	Thiencarbazone	149	0.0001
RF-0452-001-PPP	Zoxamide	281	0.0001

aka: also known as; bw: body weight; CAG: cumulative assessment group; NOAEL: no-observed adverse effect level; RD: residue definition; RPF: relative potency factor

[1] Index compound

[2] Maneb, mancozeb, metiram, propineb and ziram are approved substances and belong all to the residue definition (RD) 'dithiocarbamates (dithiocarbamates expressed as CS_2, including maneb, mancozeb, metiram, propineb, thiram and ziram)'. In the cumulative assessment, the authorised dithiocarbamate per commodity was determined, and the concentration data were assumed to refer to the less potent substance that belonged to the CAG-thyroid hormone. Note that no quantifiable concentrations of dithiocarbamates were present in the residue database.

[3] The residue data of dazomet are reported in the monitoring as dazomet (RD) with RD 'dazomet (methylisothiocyanate resulting from the use of dazomet and metam)'. Both dazomet and metam are approved. The concentrations are reported as methylisothiocyanate. In the cumulative assessment, the concentrations of dazomet (RD) were assumed to relate to the presence of metam (less potent) using a conversion factor of 1.47 (based on molecular weights). Note that no quantifiable concentrations of dazomet (RD) were present in the residue database (Appendix J).

[4] The residue data of MCPA are reported in the monitoring as MCPA (RD) with RD 'MCPA and MCPB (MCPA, MCPB including their salts, esters and conjugates expressed as MCPA)'. Both substances are approved, but MCPB is not included in the CAG-thyroid hormone. MCPB degrades into MCPA. In the cumulative assessment, the concentrations of MCPA (RD) were assumed to relate to the presence of MCPA.

[5] The residue data of quizalofop-P-tefuryl (RD) are reported in the monitoring as quizalofop (RD) with RD 'quizalofop (including quizalfop-p)'. Quizalofop is not approved, and quizalofop-p, quizalofop-p-ethyl and quizalofop-p-tefuryl are. In the cumulative assessment, the concentrations of quizalofop (RD) were assumed to refer to the presence of quizalofop-p-tefuryl. Note that quizalofop (RD) is not analysed in the monitoring programme (Appendix J).

[6] The residue data of haloxyfop-P (haloxyfop-R) are reported in the monitoring as haloxyfop-R (RD) with RD 'haloxyfop including haloxyfop-R (haloxyfop-R methyl ester, haloxyfop-R and conjugates of haloxyfop-R expressed as haloxyfop-R)'. Haloxyfop-P

(haloxyfop-R) is approved and haloxyfop is not. In the cumulative assessment, concentration data of haloxyfop-R (RD) were assumed to refer to the presence of haloxyfop-P (haloxyfop-R). Note that no quantifiable concentrations of haloxyfop-R (RD) were present in the residue database (Appendix J).

[7] The residue data of resmethrin are reported in the monitoring as resmethrin (RD) with RD 'resmethrin (resmethrin including other mixtures of constituent isomers (sum of isomers))'. In the cumulative assessment, the concentration data of resmethrin (RD) were assumed to relate to the presence of resmethrin. Note that no quantifiable concentrations of resmethrin were present in the residue database (Appendix J).

[8] The residue data of both substances are reported in the monitoring as benalaxyl (RD) with RD 'benalaxyl including other mixtures of constituent isomers including benalaxyl-M (sum of isomers)'. Both active substances are approved. In the cumulative assessment, the concentration data referring to benalaxyl (RD) were assumed to relate to the presence of benalaxyl (less potent). Note that no quantifiable concentrations of benalaxyl (RD) were present in the residue database (Appendix J).

[9] The residue data of triadimefon are reported in the monitoring as triadimefon (RD) with RD 'triadimefon and triadimenol (sum of triadimefon and triadimenol)'. Triadimenol is approved and triadimefon is not. As triadimefon degrades to triadimenol, the concentrations of triadimefon (RD) were assumed to relate to the presence of triadimenol in the cumulative assessment. As triadimenol is not part of the CAG-motor division, the concentrations were assumed to be zero.

[10] The residue data of clethodim are reported in the monitoring as clethodim (RD) with RD 'clethodim (sum of sethoxydim and Clethodim including degradation products calculated as sethoxydim)'. Clethodim is approved and sethoxydim is not. In the cumulative assessment, concentrations were assumed to refer to the presence of clethodim. The concentration data were converted to sethoxydim using a conversion factor of 1.10 (based on molecular weights). Note that no quantifiable concentrations with this residue definition were present in the residue database (Appendix J).

[11] For the commodities apple, pear, beans (with pods), tomato and strawberry, the residue data of folpet are reported in the monitoring as folpet (RD) with RD 'the sum of captan and folpet'. Both captan and folpet are approved. In cumulative assessment, the concentrations of folpet (RD) were assumed to be related to the presence of captan and subsequently set to zero as captan does not belong to the CAG-thyroid hormone.

[12] The residue data of thiametoxam are reported in the monitoring as thiametoxam (RD) with RD 'thiametoxam (sum of thiametoxam and clothianidin expressed as thiametoxam)'. In the cumulative assessment, the concentrations were assumed to refer to thiametoxam, because clothianidin has a separate RD.

Appendix E. Description of food consumption data used in the cumulative dietary exposure assessment

DNFCS-Young Children 2005/2006 (Ocké et al., 2008)
The target population of the DNFCS-Young Children 2005/2006 consisted of boys and girls aged 2 to 6 living in the Netherlands. Respondents were selected from representative consumer panels of Market Research Agency GfK. Panel characteristics, such as socio-demographic characteristics, are known to GfK. Persons in these panels participate in all types of surveys and were not specially selected on nutritional characteristics. Institutionalised persons were excluded, as well as children whose parents/carers did not have sufficient knowledge of the Dutch language. Per family, only one child was included to avoid correlations in dietary consumption patterns between children of the same family. In total, 1,634 children were invited to participate in the study, of which 1,279 consented (net response of 78%). During recruitment, the representativeness of the study population was monitored and, if necessary, the recruitment was adjusted for age and sex, education of the head of the household, level of urbanisation, place of residence and region. The study population was representative regarding socio-demographic characteristics (including region and education of the head of the household), but densely populated areas were slightly underrepresented.

The food consumption data were collected in the period October 2005 to November 2006 via a food diary on two non-consecutive days (separated by about 8 to 13 days). Parents/carers were visited at home by a trained employee of GfK. During the home visit survey materials were presented and overall instructions were given.

Portion size of the foods and meals were estimated by using photographs, domestic measures (a small and a large spoon were supplied to standardise estimates), standard units, weight and/or volume. The usual volume of cups and glasses used was measured by the carer. All days of the week were equally represented, but the winter and autumn period were slightly overrepresented compared to the spring and summer period. National and/or religious holidays or holidays of the participants were not included in the survey.

DNFCS 2007-2010 (van Rossum et al., 2011)
The target population of the DNFCS 2007-2010 consisted of people aged 7 to 69 living in the Netherlands. Pregnant and breast-feeding women, as well as institutionalised people were not included. Respondents were selected from representative consumer panels of GfK. A maximum of one person per household was included in the survey to avoid correlations in dietary consumption patterns between members of the same family. In addition, the panels only included people with sufficient knowledge of the Dutch language. In total, 5,502 individuals were invited to participate in the study, of which 3,819 consented (net response of 69%). Children were overrepresented in the study population and adults underrepresented.

The food consumption data were collected over a 3-year period from March 2007 to April 2010 via two non-consecutive 24-hour dietary recalls (separated by 2 to 6 weeks). Children aged 7 to 15 were interviewed face to face during home visits in the presence of at least one of the child's parents or carers. Participants aged 16 and over were interviewed by telephone, at dates and times unannounced to the participants.

Portion sizes of the foods consumed were quantified in several ways: by means of quantities as shown on photos in a provided picture booklet, or in household measures, standard units, by weight and/or volume. The survey covered all days of the weeks and all four seasons. National and/or religious holidays or holidays of the participants were not included in the survey.

DNFCS-Older adults 2010-2012 (Ocké et al., 2013)
The target population consisted of community-dwelling men and women aged 70 years and older, living in the Netherlands. The targeted sample size was 720, including 360 men and 360 women.

DNFCS-Older adults was a nationwide cross-sectional study, designed to be representative for region, address density and age. Data were collected from October 2010 to February 2012. Per period of four weeks, municipality, age and sex-stratified samples were drawn from the samples obtained from the Municipal Personal Records Database (GBA). In this periodic sampling, the targeted number of participants, the number of participants already recruited, response rate and the number of periods still to cover were taken into account.

The dietary assessment was based on two non-consecutive dietary record assisted 24-hour recalls, carried out by means of face-to-face interviews.

Appendix F. Exclusion of analysed samples from the cumulative exposure assessment

Pesticide residue data in fruit and vegetables submitted to EFSA are coded according to the Standard Sample Description (SSD) format. In this format, commodities are coded using the matrix code ProdCode. These matrix codes are based on the coding used in Annex I of Regulation (EC) 396/2005, last amended by Regulation (EU) No 62/2018[20]. Additionally, per analysed sample also information on the exact product analysed (ProdText) and product treatment (ProdTreat) is available. To optimize the linkage between the residue data and the food consumption data, the following results were excluded:

- In case ProdTreat equalled 'Fermentation' or 'Freezing', the residue level was removed from the dataset: no consumption of such processed foods is recorded in the food consumption database and the resulting residue levels deviated largely from those analysed in their raw counterpart. An exception was made for strawberry, peas (without pods) and beans (with pods) in combination with 'Freezing'. The residue levels found in these processed commodities were equivalent to those in their raw counterpart.
- Residue levels analysed in chilli peppers were removed, because these peppers did not belong to the 30 RACs included in the exposure assessment (section 2.4).
- Based on the information in ProdText, residue data were excluded as described in Table F-1. Pesticide residue data are reported to EFSA using the coding of the commodities as defined in Annex 1 of Regulation (EC) No 396/2005. This Annex consists of two parts:
    - Part A which includes the main commodity of a group or subgroup (e.g. tomato; second column of Table F-1)
    - Part B which includes other (minor) commodities for which the same maximum residue levels apply (e.g. goji berry; third column of Table F-1).

  When the residue data of the 'minor' commodities deviated largely from those of the main commodity and information on consumption of the 'minor' product was lacking, the pesticide residue data of the 'minor' commodity was excluded.

Table F-1. Excluded pesticide residue data

ProdCode	ProdCode Name	ProdText
P0231010A	Tomato	Cape gooseberries; Physalis; Goji berries/wolfberries; Alkekengi/Chinese lanterns/ground cherries
P0231030A	Aubergine (eggplant)	Turkey berries/devil's figs/pea eggplants; Antroewas/African eggplants/gboma

[20] Commission regulation (EC) No 2018/62 of 17 January 2018 replacing Annex I to Regulation (EC) No 396/2005 of the European Parliament and of the Council; OJ L 18.

ProdCode	ProdCode Name	ProdText
P0241010A	Broccoli	Chinese broccoli/kai-lan; Choi sum/tsoi sam; Rapini/broccoletti/broccoli raab
P0252010A	Spinach	Bitawiri; tannias/arrowleaf; elephant ears/tajer leaves; Sweet potato leaves
P0260010A	Beans (with pods)	Yardlong bean, black-eyed pea; lablab beans/hyacinth

Appendix G. Overview residue data for the substances of CAG-neurochemical

See Excel file AppendixG-H-I-J

Appendix H Overview residue data of substances of CAG-motor division

See excel file AppendixG-H-I-J

Appendix I Overview residue data of substances of CAG-calcitonin

See excel file AppendixG-H-I-J

Appendix J Overview residue data of substances of CAG-thyroid hormone

See excel file AppendixG-H-I-J

Appendix K. Assumed proportion (%) of water added at home per relevant food

Food products coded in food consumption database		Food product analysed		Proportion (%)
Code	Name	Code	Name	
A.12.02.002[a]	Juice concentrate, Raspberries		Water	80
		P0153030A	Raspberries	20
A.12.02.005	Juice concentrate, Currants (black)		Water	80
		P0154030A	Currants (red, black, white)	20
A.12.02.007	Juice concentrate, Cranberries		Water	80
		P0154020A	Cranberries	20
A.12.02.012	Juice concentrate, Sweet cherry		Water	80
		P0140020A	Cherries	20
A.12.02.013	Juice concentrate, Oranges		Water	80
		P0110020A	Oranges	20
A.13.01.001	Soft drink, fruit content		Water	50
A.13.01.001.018	Fruit soft drink, multiple vitamin, with sweetener		Water	50
A.13.02	Tea (Infusion)		Water	99.17
A.13.02.001	Black tea, infusion		Water	99.17
A.13.02.002	Green tee, infusion		Water	99.17
A.13.02.003	Fruit tee, infusion		Water	99.17
A.13.02.004	Herbal tea, infusion		Water	99.17
A.13.02.005	Instant tee powder, infusion		Water	99.17
A.13.02.006	Instant tea, liquid		Water	99.17
A.13.03	Coffee (beverage)		Water	95
A.13.03.001	Coffee drink, espresso		Water	95
A.13.03.002	Coffee drink, café Americano		Water	95
A.13.03.003	Coffee drink, cappuccino		Water	95

Food products coded in food consumption database		Food product analysed		Proportion (%)
Code	Name	Code	Name	
A.13.03.004	Coffee drink, café macchiato		Water	95
A.13.03.005	Iced coffee		Water	95
A.13.03.006	Coffee with milk (café latte, café au lait)		Water	95
A.13.03.007	Instant coffee, liquid		Water	95
A.19.10	Ready to eat soups		Water	85
A.19.10.001	Vegetable/herb soup		Water	90
A.19.10.002	Grain soup		Water	95
A.19.10.004	Meat/poultry soup		Water	77.5
A.19.10.006	Legume (beans) soup		Water	84

[a] The consumed amounts of juice concentrates in the food consumption databases were high and were therefore assumed to be reported as diluted product

Appendix L. Mapping of analysed baby food products to those coded in the food consumption database

Food product analysed		Food product coded in food consumption database	
ProdCode	ProdName	FoodEx1 Code	Food Ex1 Name
PX100000A	Food for infants and young children	A.17	Food for infants and small children
PX100004A	Infant formulae	A.17.01	Infant formulae, powder
		A.17.01.001	Infant formula, milk-based, powder
		A.17.01.002	Infant formula, hypoallergenic, powder
		A.17.01.003	Infant formula, soya-based, powder
		A.17.01.004	Infant formula, milk and soya-based, powder
		A.17.01.005	Infant formula, based on protein hydrolysates, powder
		A.17.02	Infant formulae, liquid
		A.17.02.001	Infant formula, milk-based, liquid
		A.17.02.002	Infant formula, hypoallergenic, liquid
		A.17.02.003	Infant formula, soya-based, liquid
		A.17.02.004	Infant formula, milk and soya-based, liquid
		A.17.02.005	Infant formula, based on protein hydrolysates, liquid
PX100005A	Follow-on formulae	A.17.03	Follow-on formulae, powder
		A.17.03.001	Follow-on formula, milk-based, powder
		A.17.03.002	Follow-on formula, hypoallergenic, powder
		A.17.03.003	Follow-on formula, soya-based, powder
		A.17.03.004	Follow-on formula, milk and soya-based, powder
		A.17.03.005	Follow-on formula, based on protein hydrolysates, powder
		A.17.04	Follow-on formulae, liquid
		A.17.04.001	Follow-on formula, milk-based, liquid
		A.17.04.002	Follow-on formula, hypoallergenic, liquid
		A.17.04.003	Follow-on formula, soya-based, liquid
		A.17.04.004	Follow-on formula, milk and soya-based, liquid

Food product analysed		Food product coded in food consumption database	
ProdCode	ProdName	FoodEx1 Code	Food Ex1 Name
		A.17.04.005	Follow-on formula, based on protein hydrolysates, liquid
PX100003A	Processed cereal-based foods for infants and young children	A.17.05	Cereal-based food for infants and young children
		A.17.05.001	Simple cereals which are or have to be reconstituted with milk or other appropriate nutritious liquids
		A.17.05.002	Cereals with an added high protein food which are or have to be reconstituted with water or other protein-free liquid
		A.17.05.003	Biscuits, rusks and cookies for children
		A.17.05.004	Pasta for children
PX100001A	Baby foods other than processed cereal-based foods	A.17.06	Ready-to-eat meal for infants and young children
		A.17.06.001	Ready-to-eat meal for children, vegetable-based
PX100001A	Baby foods other than processed cereal-based foods	A.17.06.003	Ready-to-eat meal for children, meat/fish-based
		A.17.06.004	Ready-to-eat meal for children, meat and vegetables
		A.17.06.005	Fruit purée for children
		A.17.07	Yoghurt, cheese and milk-based dessert for infants and young children
		A.17.07.001	Yoghurt for infants and young children
		A.17.07.002	Cheese preparations for infants and young children
		A.17.07.003	Dessert and puddings for infants and young children
		A.17.08	Fruit juice and herbal tea for infants and young children
		A.17.08.001	Fruit juice for infants and young children
		A.17.08.002	Fruit nectar for infants and young children
		A.17.08.003	Tee for infants and young children
		A.17.08.004	Tee and juice mixture for infants and young children
PX100003A	Processed cereal-based foods for infants and young children	A.17.06.002	Ready-to-eat meal for children, cereal-based

Appendix M. Use frequency data of substances of the CAG-neurochemical as retrieved from the residue database

See excel file AppendixM-N-O-P.xlsx

Appendix N. Use frequency data of substances of the CAG-motor division as retrieved from residue database

See excel file AppendixM-N-O-P.xlsx

Appendix O. Use frequency data of substances of the CAG-calcitonin as retrieved from residue database

See excel file AppendixM-N-O-P.xlsx

Appendix P. Use frequency data of substances of the CAG-thyroid hormone as retrieved from residue database

See excel file AppendixM-N-O-P.xlsx

Appendix Q. Overview of the unit weights and number of single units per sample and raw agricultural commodity (RAC) analysed

RAC[a]	Unit weight[b] (g)	Nr of units
Apples	112	20
Aubergines (egg plants)	271	10
Bananas	100	20
Broccoli	186	20
Carrots	80	20
Cauliflower	689.9	10
Courgettes	114	20
Cucumbers	411.4	10
Head cabbage	1281.9	10
Leek	168.8	20
Lettuce	534.7	10
Mandarins	100	20
Melons	540	10
Oranges	160	20
Peaches	127.6	20
Pears	206.5	20
Peppers	154.9	20
Potatoes	216	20
Table grapes (bunches)	581.55	10
Tomatoes	142.5	20

Nr: number; RAC: raw agricultural commodity

[a] For the following RACs, the unit weight was below 25 grams: cereals, beans (with pods), olives (for oil production), peas (without pods), spinach, strawberry and wine grape

[b] Taken from PRIMo rev. 2 (EFSA, 2007)

Appendix R. Margins of exposure per exposure percentile for all four CAGs and age groups

Age (years)	Margins of exposure[1] per percentile of exposure					
	P50	P90	P95	P99	P99.9	P99.99
CAG-neurochemical						
2-6	6481 (6023 – 6904)	1930 (1558 - 2240)	1098 (828 - 1447)	396 (280 - 567)	116 (54 - 181)	31 (21 - 82)
7-17	10520 (9896 - 11120)	3803 (3380 - 4349)	2444 (2018 - 3222)	881 (707 - 1245)	254 (167 - 379)	109 (52 - 214)
18-69	9624 (8998 - 10010)	4095 (3749 - 4515)	2899 (2446 - 3410)	1192 (998 - 1601)	331 (166 - 571)	114 (74 - 285)
70+	9254 (8907 - 9640)	4670 (4197 - 5058)	3442 (2916 - 3901)	1355 (1058 - 1727)	240 (89 - 536)	62 (39 - 225)
CAG-motor division						
2-6	20450 (9467 - 24470)	4742 (2488 - 5998)	3042 (1846 - 3586)	1192 (935 - 1431)	415 (327 - 567)	209 (144 - 343)
7-17	38330 (26480 - 44750)	8415 (4861 - 11400)	4906 (3119 - 6497)	1932 (1374 - 2464)	716 (546 - 932)	326 (217 - 577)
18-69	39850 (30480 - 44510)	11240 (7277 - 14110)	6861 (4720 - 8440)	2903 (2196 - 3550)	1065 (813 - 1486)	512 (352 - 962)
70+	39240 (29410 - 43500)	11630 (7045 - 14220)	6963 (4778 - 8527)	2706 (2006 - 3317)	868 (610 - 1255)	443 (353 - 895)
CAG-calcitonin						
2-6	6633 (5988 - 7109)	3223 (2942 - 3402)	2671 (2440 - 2823)	1729 (1445 - 1981)	1049 (922 - 1358)	903 (726 - 1143)
7-17	9840 (9150 - 10530)	4930 (4484 - 5221)	4097 (3905 - 4279)	3156 (2778 - 3484)	2286 (2139 - 2720)	2092 (1989 - 2597)
18-69	8788 (8264 - 9130)	4650 (4320 - 4824)	3803 (3604 - 3982)	2716 (2404 - 3045)	2112 (2004 - 2226)	1929 (1821 - 2196)
70+	8544 (8057 - 9114)	5262 (4922 - 5580)	4669 (4326 - 4978)	3625 (3421 - 3916)	2949 (2806 - 3411)	2791 (2743 - 3264)

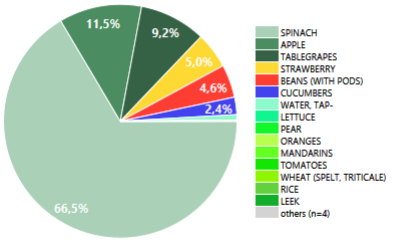
Age (years)	Margins of exposure[1] per percentile of exposure					
	P50	P90	P95	P99	P99.9	P99.99
CAG-thyroid hormone						
2-6	37500 (30420 - 47480)	16130 (13850 - 20000)	13000 (9958 - 15950)	6824 (4475 - 10270)	3126 (2151 - 5849)	3054 (2047 - 4625)
7-17	62040 (44840 - 90060)	28090 (21310 - 35820)	21610 (15180 - 27870)	12820 (9208 - 16840)	7202 (4695 - 11470)	6043 (4343 - 9369)
18-69	78110 (66490 - 97710)	34780 (28240 - 42510)	25760 (20940 - 32240)	17620 (11960 - 21590)	10710 (5410 - 15640)	6118 (3939 - 13240)
70+	71240 (60050 - 89390)	33100 (24920 - 45100)	25870 (18170 - 35160)	17330 (11700 - 24090)	13110 (8247 - 18170)	10580 (7278 - 17180)

CAG: cumulative assessment group

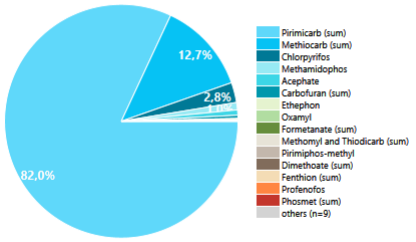
[1] Margin of exposure is the ratio between the no-observed adverse effect level (NOAEL) of the index compound of the CAG and the percentile of exposure (see section 3). This entity has therefore no dimension.

Appendix S. Contribution of raw agricultural commodities ('foods as measured'), substances ('compounds') and substance/raw agricultural commodity combinations to the upper 0.1% of the acute cumulative exposure distribution of CAG-neurochemical for the four age groups

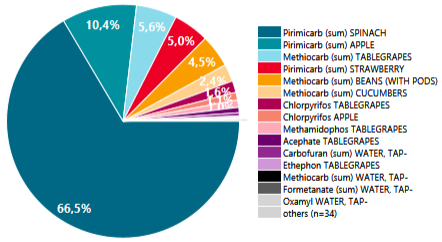
Contribution to upper exposure distribution for foods as measured



Contribution to upper exposure distribution for compounds

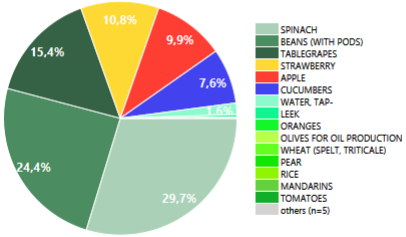


Contribution to the upper tail distribution for foods as measured x compounds (MSCC)

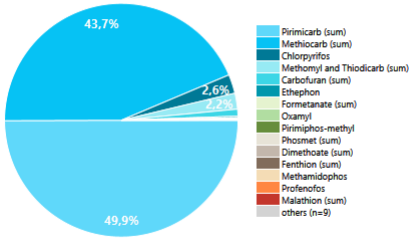


2-6 years

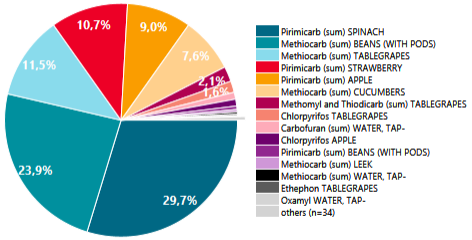
Contribution to upper exposure distribution for foods as measured



Contribution to upper exposure distribution for compounds

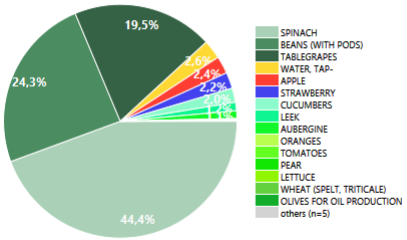


Contribution to the upper tail distribution for foods as measured x compounds (MSCC)

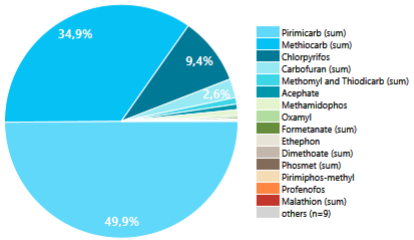


7-17 years

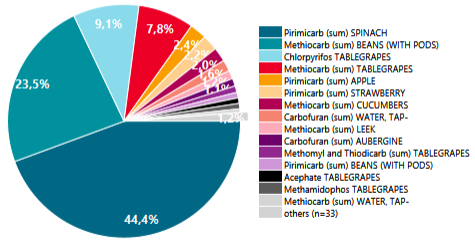
Contribution to upper exposure distribution for foods as measured



Contribution to upper exposure distribution for compounds

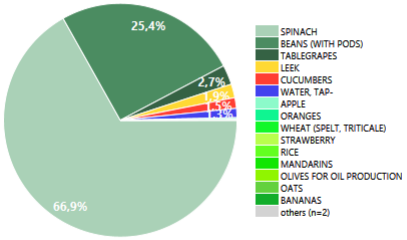


Contribution to the upper tail distribution for foods as measured x compounds (MSCC)

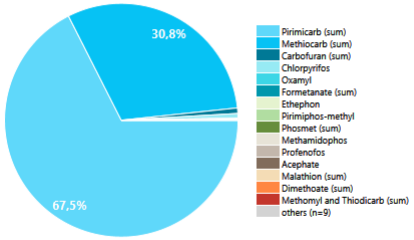


18-69 years

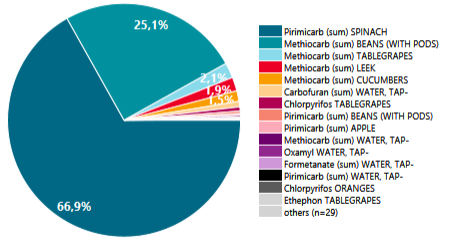
Contribution to upper exposure distribution for foods as measured



Contribution to upper exposure distribution for compounds



Contribution to the upper tail distribution for foods as measured x compounds (MSCC)

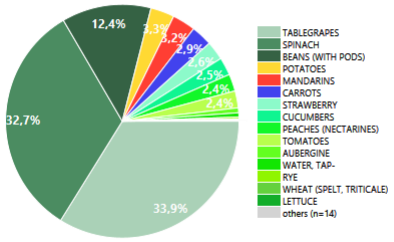


70+ years

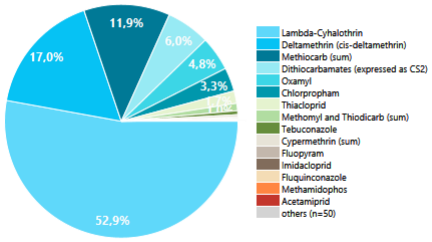
CAG: cumulative assessment group

Appendix T. Contribution of raw agricultural commodities ('foods as measured'), substances ('compounds') and substance/raw agricultural commodity combinations to the upper 0.1% of the chronic cumulative exposure distribution of CAG-motor division for the four age groups[1]

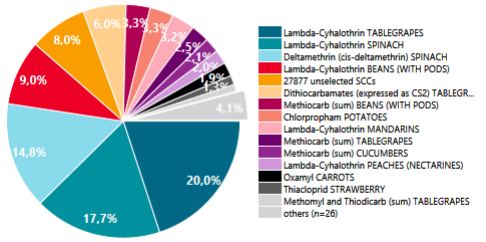
Contribution to upper exposure distribution for foods as measured



Contribution to upper exposure distribution for compounds

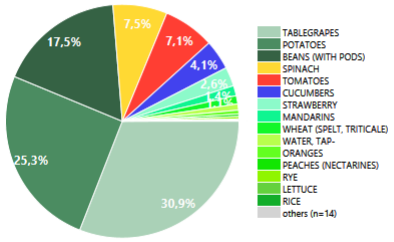


Contribution to the upper tail distribution for foods as measured x compounds (MSCC)

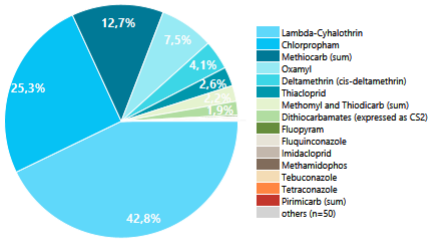


2-6 years

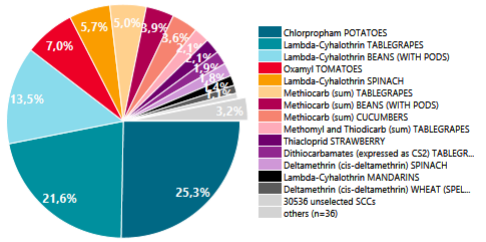
Contribution to upper exposure distribution for foods as measured



Contribution to upper exposure distribution for compounds

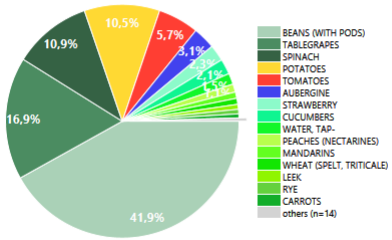


Contribution to the upper tail distribution for foods as measured x compounds (MSCC)

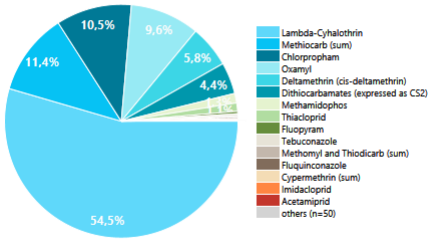


7-17 years

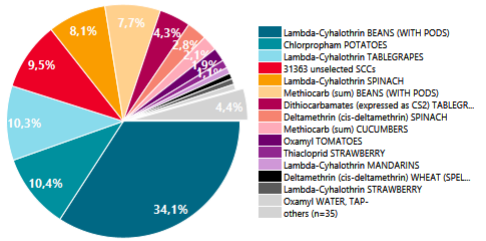
Contribution to upper exposure distribution for foods as measured



Contribution to upper exposure distribution for compounds

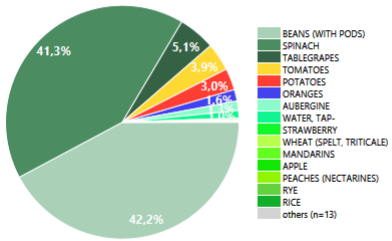


Contribution to the upper tail distribution for foods as measured x compounds (MSCC)

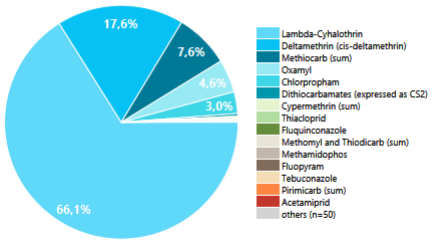


18-69 years

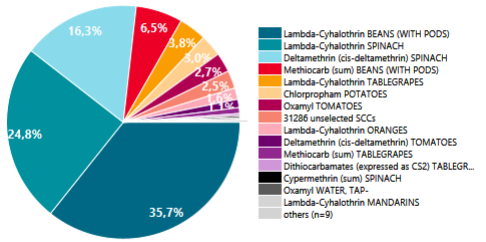
Contribution to upper exposure distribution for foods as measured



Contribution to upper exposure distribution for compounds



Contribution to the upper tail distribution for foods as measured x compounds (MSCC)



70+ years

CAG: cumulative assessment group

[1] The contributions for foods as measured x compounds related to 'unselected SCCs' refer to the sum of many very small contributions. The amount refers to the number of combinations.

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